L5 ANSWER 19 OF 22 MEDLINE
AN 96103035 MEDLINE
DN 96103035
TI Role of endogenous bradykinin in human coronary vasomotor control.
AU Groves P; Kurz S; Just H; Drexler H
CS Medizinische Klinik III, Universitat Freiburg, Germany.
SO CIRCULATION, (1995 Dec 15) 92 (12) 3424-30.
Journal code: DAW. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199603
AB BACKGROUND: Bradykinin is a potent vasodilator that acts through B2 kinin receptors to stimulate the release of endothelium-derived nitric oxide, prostacyclin, and hyperpolarizing factor. In this study, we investigated the contribution of endogenous bradykinin to vasomotor control in the human coronary circulation. METHODS AND RESULTS: The selective **bradykinin B2 receptor antagonist** HOE 140 was infused into the left main coronary artery (200 micrograms/min for 15 minutes) in 15 patients without significant coronary stenoses. Epicardial responses were evaluated by quantitative coronary blood flow with a Doppler flow-velocity wire. Flow-dependent dilation (n = 10; intracoronary papaverine) and acetylcholine responses (n = 5) were assessed before and after HOE 140. After HOE 140, there was a reduction in luminal area in the proximal (P < .001), mid (P < .001), and distal (P < .05) coronary arteries. HOE 140 led to an increase in coronary vascular resistance (P < .001) and a decrease in coronary blood flow (P < .001). After bradykinin B2 receptor blockade, there was a reduction in flow-dependent dilation (23.4 +/- 6.9% to 3.9 +/- 6.0%, P < .001), the extent of which correlated with the degree of basal vasoconstriction after HOE 140 in the same vessel segment (P < .05). Acetylcholine responses were unchanged after HOE 140. CONCLUSIONS: The results of this study demonstrate for the first time a role for endogenous bradykinin in mediating normal vasomotor responses in resistance and epicardial coronary vessels under basal and flow-stimulated conditions in the human coronary circulation.

L5 ANSWER 20 OF 22 MEDLINE
AN 95203597 MEDLINE
DN 95203597
TI Captopril increases skin microvascular blood flow secondary to bradykinin, nitric oxide, and prostaglandins.
AU Warren J B; Loi R K
CS Department of Applied Pharmacology, National Heart and Lung Institute, London, United Kingdom..
SO FASEB JOURNAL, (1995 Mar) 9 (5) 411-8.
Journal code: FAS. ISSN: 0892-6638.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals

ANSWER 333 OF 417 MEDLINE

AN 75221359 MEDLINE

DN 75221359

TI Superior mesenteric blood flow in man following injection of bradykinin and vasopressin into the superior mesenteric artery.

AU Norryd C; Dencker H; Lunderquist A; Olin T

SO ACTA CHIRURGICA SCANDINAVICA, (1975) 141 (2) 119-28.
Journal code: 0KA. ISSN: 0001-5482.

CY Sweden

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 197512

AB The superior mesenteric blood flow was studied with a dye-dilution technique after catheterization of the superior mesenteric artery and vein. The investigation was performed in connection with portography in 22 patients with apparently normal small bowel function. Intra-arterial injection of 5, 10 or 20 mug bradykinin was followed within one minute by an increase, on the average, of 114, 176 and 223% respectively, in the superior mesenteric blood flow. The blood flow was dose-dependent in this range. The estimated vascular resistance decreased by 52, 61 and 67%, respectively. The portal venous pressure was increased slightly after intra-arterial injection, but the pressure was unchanged after intra-portal injection. Intra-arterial injection of bradykinin causes a highly improved venous phase at superior mesenteric angiography. This may be due not only to the increased flow but to some extent also to increased capillary permeability produced by bradykinin. Intra-arterial injection of 0.125 and 0.250 IU of vasopressin decreased the superior mesenteric blood flow by 53 and 54%, respectively, within 3 minutes of the injection. The dye-dilution method used was not applicable to blood flow below a level of about 200 ml/min. Continuous infusion of 0.05 IU/min decreased the superior mesenteric blood flow by, on an average, 58%. The portal venous pressure was decreased by 25% after the intra-arterial injection, but no change in pressure was recorded after intra-portal administration. The clinical use of intra-arterial infusion of vasopressin during gastrointenstinal bleeding is discussed.

9 ANSWER 2010 OF 2045 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1977:230308 BIOSIS
DN BA64:52672
TI MORPHINE FAILS TO BLOCK THE DISCHARGES EVOKED BY **INTRA ARTERIAL** BRADY KININ IN DORSAL HORN NEURONS OF SPINAL CATS.
AU PIERCEY M F; HOLLISTER R P
SO NEUROPHARMACOLOGY, (1977) 16 (6), 425-429.
CODEN: NEPHBW. ISSN: 0028-3908.
FS BA; OLD
LA Unavailable
AB Microelectrodes were used to record the electrical activity of single neurons in the dorsal horn of spinal cats. Morphine (1-3 mg/kg i.v.) reduced the spontaneous and electrically-evoked discharges of dorsal horn neurons. Morphine reduced the excitatory discharges evoked by **intra-arterial bradykinin** in only 1 of 7 neurons tested. Only a portion of morphine's analgesic activity resulted from a direct action on dorsal horn neurons.

9 ANSWER 2016 OF 2045 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1977:193564 BIOSIS
DN BA64:15928
TI RESPONSES OF THORACIC DORSAL HORN INTER NEURONS TO CUTANEOUS STIMULATION AND TO THE **ADMINISTRATION** OF ALGOGENIC SUBSTANCES INTO THE MESENTERIC ARTERY IN THE SPINAL CAT.
AU GUILBAUD G; BENELLI B; BESSON J M
SO BRAIN RES, (1977) 124 (3), 437-448.
CODEN: BRREAP. ISSN: 0006-8993.
FS BA; OLD
LA Unavailable
AB The effects of the injection of algogenic substances (**bradykinin**, acetylcholine) into the inferior mesenteric artery were studied at the thoracic level on 47 dorsal horn interneurons responding to cutaneous stimulation. Each unit was characterized by its electrophysiological properties and carefully located within the cord by extracellular injection of pontamine sky blue. Twenty cells, driven only by non-noxious cutaneous stimulation and mainly located in lamina IV, were not affected by the **administration** of algogenic substances. The activity of 25/27 cells, excited by both non-noxious and noxious cutaneous stimulation and mainly located in lamina V, was strongly modified by nociceptive visceral stimulation, induced by **bradykinin** and acetylcholine: 8/27 cells were activated, 14/27 were inhibited and 3/27 had a mixed inhibitory-excitatory response. It appeared that nociceptive visceral messages only project on dorsal horn cells receiving noxious cutaneous afferents. Viscerosomatic convergence seems only to concern nociceptive messages; this kind of convergence reinforces the hypothesis explaining referred pain from a neurophysiological point of view.

L9 ANSWER 2028 OF 2045 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1977:122375 BIOSIS
DN BA63:17239
TI SECRETORY AND MOTOR EFFECTS IN THE SUBMAXILLARY GLAND OF THE RAT ON **INTRA ARTERIAL ADMINISTRATION** OF SOME POLY PEPTIDES AND AUTONOMIC DRUGS.
AU THULIN A
SO ACTA PHYSIOL SCAND, (1976) 97 (3), 343-348.
CODEN: APSCAX. ISSN: 0001-6772.
FS BA; OLD
LA Unavailable
AB **Bradykinin**, oxytocin, physalaemin and some autonomic drugs were injected into the common carotid artery. Physalaemin evoked secretion and a pressure rise in the submaxillary duct. A duct pressure rise could be elicited by **bradykinin** which did not evoke secretion. Autonomic blocking agents did not diminish secretion evoked by physalaemin and did not change pressure responses elicited by **bradykinin** or physalaemin. Neither secretion, nor duct pressure changes could be recorded after **administration** of oxytocin. Secretion evoked by autonomic drugs was mediated via cholinergic, .alpha.- and .beta.-adrenergic receptors, while motor effects were due to activation of cholinergic and .alpha.-adrenergic receptors.

ANSWER 1038 OF 2045 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1993:582481 BIOSIS

DN PREV199497001851

TI In **vivo** B-2-receptor-mediated negative chronotropic effect of **bradykinin** in canine sinus node.

AU Ribuot, Christophe; Godin, Diane; Couture, Rejean; Regoli, Domenico; Nadeau, Reginald (1)

CS (1) Res. Center, Hopital du Sacre-Coeur de Montreal, 5400 Gouin Blvd., Montreal, PQ H4J 1C5 Canada

SO American Journal of Physiology, (1993) Vol. 265, No. 3 PART 2, pp. H876-H879.
ISSN: 0002-9513.

DT Article

LA English

AB The chronotropic response to **bradykinin** (BK) injected into the sinus node artery was evaluated in anesthetized dogs. The animals (n = 14) were vagotomized and pretreated with propranolol (1 mg/kg iv) to prevent baroreceptor-mediated effects. Dose-dependent decreases in heart rate (from 2.4 +- 1.3% for 1 mu-g of BK to 13.1 +- 3.7% for 10 mu-g of BK), as well as a significant fall in systemic systolic and diastolic blood pressures, were observed. Captopril (2 mg/kg iv) caused significant decreases in systolic (from 117 +- 11 to 77 +- 12 mmHg, P lt 0.001) and diastolic (from 87 +- 8 to 52 +- 8 mmHg, P lt 0.001) blood pressures but had no effect on heart rate. Converting-enzyme inhibition potentiated the BK-induced bradycardia. The new potent B-2-receptor antagonist, HOE 140 (100 mu-g), significantly blocked the BK-induced chronotropic effect, whereas desArg-9-BK, a B-1-receptor agonist, was without effect. Prostaglandin involvement was excluded, since pretreatment with indomethacin did not prevent the bradycardia. In conclusion, in **vivo** BK induces a direct negative chronotropic effect, which is potentiated by converting-enzyme inhibition and is mediated by the B-2-receptors independently of the prostaglandins.

ANSWER 1029 OF 2045 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1994:15933 BIOSIS

DN PREV199497028933

TI Purification of a vasoactive peptide related to lysyl-**bradykinin** from trout plasma.

AU Conlon, J. Michael (1); Olson, Kenneth R.

CS (1) Regulatory Peptide Cent., Dep. Biomed. Sci., Creighton Univ. Sch. Med., Omaha, NE 68178 USA

SO FEBS (Federation of European Biochemical Societies) Letters, (1993) Vol. 334, No. 1, pp. 75-78.
ISSN: 0014-5793.

DT Article

LA English

AB Incubation of plasma from the steelhead trout, Oncorhynchus mykiss with porcine pancreatic glandular kallikrein generated **bradykinin** -like immunoreactivity. The primary structure of the immunoreactive peptide was established as: Lys-Arg-Pro-Pro-Gly-Trp-Ser-Pro-Leu-Arg. This sequence shows two amino acid substitutions (Phe-6 fwdarw Trp and Phe-9 fwdarw Leu) compared with mammalian lysyl-**bradykinin** (kallidin), Bolus **intraarterial** injection of the purified peptide produced a strong and sustained vasopressor response in the unanaesthetized trout. The data demonstrate that the kallikrein-kinin system predates the appearance of tetrapods and suggest a role for this system in cardiovascular regulation in fish.

7 ANSWER 264 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1986:199721 BIOSIS
DN BA81:91021
TI EFFECT OF VASOACTIVE PEPTIDES ON PROSTACYCLIN SYNTHESIS IN MAN.
AU BARROW S E; DOLLERY C T; HEAVEY D J; HICKLING N E; RITTER J M; VIAL J
CS DEP. CLINICAL PHARMACOLOGY, ROYAL POSTGRADUATE MED. SCH., LONDON W12 0HS.
SO BR J PHARMACOL, (1986) 87 (1), 243-248.
CODEN: BJPCBM. ISSN: 0007-1188.
FS BA; OLD
LA English
AB 1 **Bradykinin**, angiotensin II, arginine vasopressin (AVP) or des-amino-D-arginine vasopressin (DDAVP) were administered by **intravenous** infusion to 10 healthy men. 2 The concentration of 6-oxo-prostaglandin F1.alpha. (6-oxo-PGF1.alpha.), the stable hydrolysis product of prostacyclin (PGI2), was measured in plasma using gas chromatography/negative ion chemical ionisation mass spectrometry. 3 Dose-related increases in plasma concenrations of 6-oxo-PGF1.alpha. occurred during administration of **bradykinin** (100-3200 ng kg-1 min-1). The concentrations of 6-oxo-PGF1.alpha. rose from baseline values in the range < 1.0-4.9 pg ml-1 to 24.9-47.6 pg ml-1 at maximum tolerated infusion rates. 4 There were no changes in the concentrations of 6-oxo-PGF1.alpha. during administration of angiotensin II, AVP or DDAVP at infusion rates which caused haemodynamic changes.

ANSWER 258 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1986:337183 BIOSIS
DN BA82:51387
TI VAGAL INVOLVEMENT IN THE PRESSOR RESPONSES TO CRANIAL ARTERY INFUSIONS OF **BRADYKININ** IN ANESTHETIZED GREYHOUNDS.
AU WILKINSON D L; SCROOP G C
CS DEP. PHYSIOLOGY, UNIV. ADELAIDE, ADELAIDE, SOUTH AUSTRALIA 5000.
SO EUR J PHARMACOL, (1986) 123 (3), 409-414.
CODEN: EJPHAZ. ISSN: 0014-2999.
FS BA; OLD
LA English
AB In anaesthetised greyhounds, vertebral and carotid artery infusions of **bradykinin** increased blood pressure whereas **intravenous** infusions caused a decrease. With each route of administration, heart rate and cardiac output increased while total peripheral resistance fell. With cranial artery infusions, the consecutive pretreatments of propranolol, phentolamine and vagal cooling resulted in a progressive reduction in the heart rate responses and conversion of the pressor to depressor responses. The responses to **intravenous** infusions of **bradykinin** were little changed. In contrast, when the initial pretreatment was interruption of vagal transmission, cranial artery infusions of **bradykinin** were at once depressor and the depressor response to **intravenous** infusions immediately enhanced. Subsequent propranolol and phentolamine were without further effect on the blood pressure responses although propranolol did reduce the tachycardia responses. It is concluded that while the tachycardia induced by cranial artery infusions of **bradykinin** has both cardiac sympathetic and vagal withdrawal components, the hypertensive action is mediated by an increase in cardiac output due largely to withdrawal of cardiac vagal tone.

ANSWER 249 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1988:109697 BIOSIS

DN BA85:55167

TI INCREASED SKIN LYMPH PROTEIN CLEARANCE AFTER A 6-H ARTERIAL **BRADYKININ** INFUSION.

AU MULLINS R J; HUDGENS R W

CS DEP. SURG., UNIV. LOUISVILLE, LOUSIVILLE, KY. 40202.

SO AM J PHYSIOL, (1987) 253 (6 PART 2), H1462-H1469.
CODEN: AJPHAP. ISSN: 0002-9513.

FS BA; OLD

LA English

AB When **bradykinin** (0.15-0.28 .mu. .cntdot. kg-1 .cntdot. min-1) was infused into both femoral arteries of 11 anesthetized dogs, skin lymph flows increased by 25-371% within 2 h, and mean lymph protein concentrations increased by one-third. To determine whether, in addition to the initial increase in permeability, a 6.5- to 10-h **bradykinin** infusion caused a sustained effect, the **bradykinin** infusion into one hindpaw was stopped after 2 h (2HR), whereas the contralateral hindpaw was infused continuously (CONT). Two hours after the **bradykinin** infusion was stopped, Ringer lactate equal to 10% of the dog's body weight was given intravenously to further increase lymph flow. After Ringer lactate infusion, increase in lymph protein clearance fromthe CONT hindpaws wasgreater than that from the 2HR hindpaws (change is clearance from before Ringer lactate infusion final: 2HR, 6.9 .+-. 1.4 to 8.8 .+-. 1.1; CONT, 23.4 .+-. 2.5 to 40.2 .+-. 4.8 .mu.l/min). In the final lymph samples of the CONT, but not 2HR, hindpaws, the lymph-to-plasma ratio for immunoglobulin G and immunoglobulin M divided by the albumin lymph-to-plasma ratio exceeded the value of these ratios in the base-line samples. An **intravenous** bolus of Evans blue dye was given < 2 h before the end of the experiment. The concentrations of dye in the final lymph samples wee greater in CONT hindpaws (12.6 .+-. 3.7% plasma equivalents) than in the 2HR hindpaws (1.1 .+-. 0.5%). A continuous 6.5- to 10-h intra-arterial **bradykinin** infusion produced a sustained increase of transvascular protein clearance in skin that is consistent with a sustained increased in microvascular membrane permeability.

WER 247 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1988:136688 BIOSIS
DN BA85:71515
TI **BRADYKININ**-STIMULATED PROSTAGLANDIN SYNTHESIS IN CONSCIOUS RABBITS.
AU WARREN J B; RITTER J M; HICKLING N E; BARROW S E
CS DEP. CLINICAL PHARMACOL., ROYAL POSTGRADUATE MED. SCH., DUCANE ROAD, LONDON W12 0HS.
SO BR J PHARMACOL, (1987) 92 (4), 895-900.
CODEN: BJPCBM. ISSN: 0007-1188.
FS BA; OLD
LA English
AB 1 **Bradykinin** was infused intravenously into conscious rabbits to determine its effect on the concentration of prostaglandins in plasma. 6-Oxo-prostaglandin (PG) F1.alpha., the stable hydrolysis product of prostacyclin, and 13,14-dihydro-15-oxo-PGF2.alpha., a metabolite derived from PGE2 and PGF2.alpha., were measured by gas chromatography-electron capture mass spectrometry. 2 Incremental infusions of **bradykinin** (0.4-3.2 .mu.g kg-1 min-1) increased plasma concentrations of both 6-oxo-PGF1.alpha. and 13,14-dihydro-15-oxo-PGF2.alpha.. 3 Aspirin (10 mg kg-1, i.v.) inhibited **bradykinin**-stimulated 6-oxo-PGF1.alpha. and 13,14-dihydro-15-oxo-PGF2.alpha. synthesis at 30 min at 6 h. At 24 h, the mean **bradykinin**-stimulated 13,14-dihydro-15-oxoPGF2.alpha. concentration was 66% of its original value, whilst 6-oxo-PGF1.alpha. remained substantially inhibited. 4 The different rates of recovery of **bradykinin**-stimulated production of the two prostaglandins after inhibition by aspirin suggests that **intravenous** **bradykinin** stimulates prostacyclin and PGE2/PGF2.alpha. production in distinct cell populations which synthesize cyclo-oxygenase at different rates.

ANSWER 231 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1989:341112 BIOSIS

DN BA88:44112

TI INHIBITION OF **BRADYKININ**-INDUCED BRONCHOCONSTRICTION IN THE GUINEA-PIG BY A SYNTHETIC B-2 RECEPTOR ANTAGONIST.

AU JIN L S; PAGE C P; SCHACHTER M

CS DEP. OF PHARMACOL., KING'S COLL., CHELSEA CAMPUS, UNIV. OF LONDON, MANRESA RD., SW3 6LX.

SO BR J PHARMACOL, (1989) 97 (2), 598-602. CODEN: BJPCBM. ISSN: 0007-1188.

FS BA; OLD

LA English

AB 1 **Intravenous bradykinin** (Bk) elicited bronchoconstriction in the anaesthetized ventilated guinea-pig which was not mimicked by the B1 receptor agonist, des-Arg9-Bk. 2 **Bradykinin** -induced bronchoconstriction was inhibited by the B2 receptor antagonist B4881, but not by the B1 receptor antagonist des-Arg9-Leu8-Bk. The effect of B4881 was short-lived. 3 The B2 receptor antagonist as B4881 was selective for **bradykinin** as B4881 did not significantly inhibit bronchoconstriction induced by i.v. bombesin, platelet activating factor, acetylcholine, histamine or vagal stimulation. 4 These results suggest that **bradykinin**-induced bronchoconstriction in the guinea-pig is via activation of a B2 receptor population and that B4881 is a selective B2 antagonist that may be useful for investigating the involvement of **bradykinin** in the lung.

L7 ANSWER 227 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1990:25213 BIOSIS
DN BA89:12179
TI MODULATION OF THE VASODEPRESSOR ACTIONS OF ACETYLCHOLINE **BRADYKININ** SUBSTANCE P AND ENDOTHELIN IN THE RAT BY A SPECIFIC INHIBITOR OF NITRIC OXIDE FORMATION.
AU WHITTLE B J R; LOPEZ-BELMONTE J; REES D D
CS DEP. PHARMACOLOGY, WELLCOME RES. LAB., LANGLEY COURT, BECKENHAM, KENT BR3 3BS.
SO BR J PHARMACOL, (1989) 98 (2), 646-652.
CODEN: BJPCBM. ISSN: 0007-1188.
FS BA; OLD
LA English
AB The effects of the specific inhibitor of nitric oxide (NO) formation, NG-monomethyl-L-arginine (L-NMMA), on resting systemic arterial blood pressure (BP) and on the actions of both endothelium-dependent and endothelium-independent vasodilators were investigated in the anaesthetized, normotensive rat. **Intravenous** administration of L-NMMA (12.5-50 mg kg-1; 47-188 .mu.mol kg-1) but not its enantiomer, D-NMMA, induced a dose-related increase in BP, which was reversed by the **intravenous** administration of L-arginine (150-600 .mu.mol kg-1), but not D-arginine. The vasodepressor responses to **intravenous** administration of the endothelium-dependent vasodilators, acetylcholine, **bradykinin** and substance P were significantly inhibited by L-NMMA (94 and 188 .mu.mol kg-1 i.v.), but not by D-NMMA. The inhibition by L-NMMA of these vasodepressor responses was reversed by administration of L-arginine, but not D-arginine. Endothelin (ET-1) induced dose-related vasodepressor responses following bolus **intravenous** administration, which were significantly inhibited by L-NMMA but not by D-NMMA. This inhibition was reversed by administration of L-arginine. The vasodepressor effects of the endothelium-independent vasodilators, glyceryl trinitrate or prostacyclin, were not significantly inhibited by L-NMMA. These findings with L-NMMA suggest that resting blood pressure in the rat is modulated by endogenous NO biosynthesis and that endothelium-dependent vasodilators act through the formation of endogenous NO to exert their actions in vivo.

ANSWER 218 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1990:411561 BIOSIS

DN BA90:72362

TI ROLE OF **BRADYKININ** IN THE REGULATION OF BLOOD PRESSURE AND RENAL BLOOD FLOW IN DOCA-SALT HYPERTENSIVE RATS.

AU SEINO M; ABE K; NUSHIRO N; OMATA K; KASAI Y; TSUNODA K; KANAZAWA M; YOSHIDA K; YOSHINAGA K

CS THE SECOND INTERN. MED., YOHOKU UNIV. SCH. MED., 1-1 SEIRYOCHO, SENDAI 980, JAPAN.

SO J HYPERTENS, (1990) 8 (5), 411-416.
CODEN: JOHYD3. ISSN: 0263-6352.

FS BA; OLD

LA English

AB We examined the role of **bradykinin** in the onset and/or the maintenance of blood pressure and renal blood flow in deoxycorticosterone acetate (DOCA)-salt hypertension rats by using a competitive antagonist of **bradykinin** [Arg-Pro-Hyp-Gly-Thi-Ser-Dphe-Thi-Arg; Hyp, L-4-hydroxyproline; Thi, .beta.-(2-theinyl-L-alanine)]. The **intravenous** injection of the **bradykinin** antagonist (25, 50, and 100 .mu.g) produced an increase in mean arterial pressure in all rats treated with tap water, 1% NaCl and DOCA + 1% NaCl. However, the magnitude of the increase in mean arterial pressure was significantly lower in the DOCA-hypertensive rats than in two groups of rats drinking tap water and 1% NaCl after 4 and 6 weeks, but there was no significant difference after 2 weeks. The **bradykinin** antagonist induced a decrease in renal blood flow in all rats. However, the extent of the fall in renal blood flow was reduced in the DOCA-hypertensive rats compared with the control rats drinking tap water. These results suggest that endogenous **bradykinin** is depressed in the established phase of hypertension in DOCA-hypertensive rats. It is also suggested that endogenous **bradykinin** may counteract the elevation of vascular resistance in the early stages of this model.

ANSWER 208 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1991:347676 BIOSIS

DN BA92:47051

TI THE ACTIONS OF **BRADYKININ** AND LYSINE **BRADYKININ** ON TRACHEAL BLOOD FLOW AND SMOOTH MUSCLE IN ANESTHETIZED SHEEP.

AU CORFIELD D R; WEBBER S E; HANAFI Z; WIDDICOMBE J G

CS DEP. PHYSIOL., ST. GEORGE'S HOSPITAL MED. SCH., CRANMER TERRACE, LONDON SW17 0RE.

SO PULM PHARMACOL, (1991) 4 (2), 85-90.
CODEN: PUPHEX. ISSN: 0952-0600.

FS BA; OLD

LA English

AB The actions of **bradykinin** and the related compound lys-**bradykinin** have been studied on the tracheal circulation and tracheal smooth muscle of the sheep. Cranial tracheal arteries of ten anaesthetised and paralysed sheep were isolated and perfused at systemic arterial pressure; arterial inflow was measured with an electromagnetic flow probe. Tracheal smooth muscle tone was assessed by measuring the external diameter of the cranial trachea. Close arterial injection of **bradykinin** and lys-**bradykinin** (0.1 to 1000 pmoles) produced potent dose-dependent falls in tracheal vascular resistance: for **bradykinin** a maximum fall of -56.4% (52.3-60.5%, 95% confidence interval) and for lys-**bradykinin** -52.8% (46.5-59.1%). The ED50 values were 0.69 (0.51-1.32) and 1.46 (1.19-2.28) pmoles respectively. Small and inconsistent relaxation of tracheal smooth msucle was seen with the higher doses (> 1.9 pmoles) of both kinins. **Intravenous** indomethacin (5mg.cntdot.kg-1) increased in vasodilation produced by **bradykinin** and lys-**bradykinin**. Oxyhaemoglobin (4 .mu.m at 0.35ml.cntdot.min-1) infused into the tracheal circulation almost abolished the responses to **bradykinin** and methacholine. The results indicate that in the sheep trachea **bradykinin** has little action on airway smooth muscle but is a potent dilator of the vasculature; **bradykinin** and lyis-**bradykinin** are of similar potency suggesting the action may be via B2 receptors. While the vascular responses may be modulated by vasoconstrictor cyclo-oxygenase products the vasodilation is likely to be endothelium-dependent and not prostanoid-mediated.

L

ANSWER 206 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1991:361669 BIOSIS

DN BA92:49894

TI INTERACTION OF **BRADYKININ** AND ANGIOTENSIN IN THE REGULATION OF BLOOD PRESSURE IN CONSCIOUS RATS.

AU VAN DEN BUUSE M; KERKHOFF J

CS MARION MERRELL DOW RES. INST., STRASBOURG RES. CENT., 16 RUE D'ANKARA, 67009 STRASBOURG CEDEX, FR.

SO GEN PHARMACOL, (1991) 22 (4), 759-762.
CODEN: GEPHDP. ISSN: 0306-3623.

FS BA; OLD

LA English

AB 1. The interaction between **bradykinin** (BK) and the renin-angiotensin system was studied in conscious, catheterized rats. 2. **Intravenous** injection of BK induced dose-dependent decreases in blood pressure in normotensive Wistar and Wistar-Kyoto rats and spontaneously hypertensive rats. Pretreatment with the angiotensin-converting enzyme (ACE) inhibitor captopril markedly enhanced the effect of BK, such that the dose-response curve shifted significantly to the left in all three strains. 3. In a second series of experiments, captopril did not change basal blood pressure, but blocked the pressor response to angiotensin I (AI), but not angiotensin II (AII). 4. The partial agonist Star1-Ala8-angiotensin II (SAR) increased blood pressure and blocked the pressor response to subsequent AII treatment. 5. After pretreatment with BK (50 .mu.g/kg), captopril evoked a decrease in blood pressure, while still blocking the effect of AI. 6. After pretreatment with BK, SAR decreased blood pressure, while still antagonizing the action of AII. 7. These results suggest that ACE plays a role in the inactivation of circulating BK in normotensive and hypertensive rats. Conversely, BK can influence the activity of the renin-angiotensin system, probably by interacting with ACE.

ANSWER 185 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1992:505977 BIOSIS

DN BA94:124502

TI DIFFERENTIAL EFFECTS OF GENERAL ANESTHESIA ON CGMP-MEDIATED PULMONARY VASODILATION.

AU MURRAY P A; FEHR D M; CHEN B B; ROCK P; ESTHER J W; DESAI P M; NYHAN D P

CS DEP. ANESTHESIOLOGY/CRITICAL CARE MEDICINE, JOHNS HOPKINS HOSPITAL, 600 N.
WOLFE ST., BALTIMORE, MD. 21205.

SO J APPL PHYSIOL, (1992) 73 (2), 721-727.
CODEN: JAPHEV. ISSN: 8750-7587.

FS BA; OLD

LA English

AB We investigated the effects of an **intravenous** (pentobarbital sodium) and an inhalational (halothane) general anesthetic on guanosine 3',5'-cyclic monophosphate- (cGMP) mediated pulmonary vasodilation compared with responses measured in the conscious state. Multipoint pulmonary vascular pressure-flow plots were generated in the same nine dogs in the fully conscious state, during pentobarbital sodium anesthesia (30 mg/kg iv), and during halothane anesthesia (.apprx. 1.2% end tidal). Continuous **intravenous** infusions of **bradykinin** (2 .mu.g .cntdot. kg-1 .cntdot. min-1) and sodium nitroprusside (5 .mu.g .cntdot. kg-1 .cntdot. min-1) were utilized to stimulate endothelium-dependent and -independent cGMP-mediated pulmonary vasodilation, respectively. In the conscious state, both **bradykinin** and nitroprusside decreased ($P < 0.01$) the pulmonary vascular pressure gradient (pulmonary arterial pressure - pulmonary arterial wedge pressure) over the entire range of flows studied; i.e., **bradykinin** and nitroprusside caused active flow-independent pulmonary vasodilation. Pulmonary vasodilator responses to **bradykinin** ($P < 0.01$) and nitroprusside ($P < 0.05$) were also observed during pentobarbital anesthesia. In contrast, during halothane anesthesia, the pulmonary vasodilator responses to both **bradykinin** and nitroprusside were abolished. These results indicate that, compared with the conscious state, cGMP-mediated pulmonary vasodilation is preserved during pentobarbital anesthesia but is abolished during halothane anesthesia.

L7 ANSWER 178 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1993:302357 BIOSIS
DN PREV199396020582
TI Modification of the renal response to endopeptidase inhibition and atrial natriuretic peptide infusion in normal dogs.
AU Levy, Mortimer (1); Cernacek, Peter
CS (1) Dep. Physiol., McGill Univ., 3655 Drummond St., Rm. 1228, Montreal, Que. H3G 1Y6 Canada
SO Canadian Journal of Physiology and Pharmacology, (1992) Vol. 70, No. 12, pp. 1563-1570.
ISSN: 0008-4212.
DT Article
LA English
SL English; French
AB Inhibition of intrarenal neutral endopeptidase 24:11 (NEP) increases the natriuretic response in infused atrial natriuretic peptide (ANP). In various models of canine heart failure, angiotensin and kinins have been shown to modulate ANP and (or) NEP activity. In the present study, we examined possible modulators of NEP activity in normal dogs by infusing various agents into the left renal artery (or by denervating the left kidney) and comparing the response of this kidney with that of the contralateral one following the combined **intravenous** infusion of Squibb 28603 (a potent NEP inhibitor) and ANP (75 ng cntdot kg-1 cntdot min-1). Four dogs received angiotensin (1.5 ng cntdot kg-1 cntdot min-1) into the left renal artery, 8 dogs received saralasin (5 mu-g/min), 5 dogs received noradrenaline (2 mu-g/min), and 6 dogs received **bradykinin** (3 mu-g/min). Five dogs underwent left renall denervation. Angiotensin inhibited sodium excretion following the NEP inhibitor alone and after the NEP inhibitor plus ANP. Saralasin augmented the natriuretic response. None of the other protocols influenced sodium excretion. We conclude that angiotensin may modulate either the enzymatic degradation of ANP or influence its renal tubular effects.

L

ANSWER 177 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1993:302623 BIOSIS
DN PREV199396020848
TI The effects of ketamine on the excitation and inhibition of dorsal horn WDR neuronal activity induced by **bradykinin** injection into the femoral artery in cats after spinal cord transection.
AU Nagasaka, Hiroshi (1); Nagasaka, Ikuko; Sato, Isao; Matsumoto, Nobuyuki; Matsumoto, Isao; Hori, Takao
CS (1) Dep. Anesthesiol., Saitama Med. Sch., 38, Morohongo, Moroyamacho, Iruma-gun, Saitama 350-04 Japan
SO Anesthesiology (Hagerstown), (1993) Vol. 78, No. 4, pp. 722-732. ISSN: 0003-3022.
DT Article
LA English
AB Background: It is now well established that wide dynamic range neurons (WDR) can possess widespread cutaneous inhibitory receptive fields, as well as excitatory receptive fields, in specific regions of the body. The ability of ketamine to depress the excitatory responses of spinal WDR neurons indicates that the analgesia produced by this agent may be a result, in part, of this spinal action. The primary purpose of this study was to investigate the effects of ketamine on the WDR propriospinal inhibitory mechanism that is induced by a **bradykinin** (BK) injection as a noxious test stimuli. Methods: In decerebrate, spinal cord-transected cats (L1-L2), the effects of a low (0.5 mg cntdot kg-1, **intravenous**) and a high (10 mg cntdot kg-1, **intravenous**) dose of ketamine on the neuronal activity of spinal dorsal horn WDR neurons evoked by femoral artery injection of BK (10 mu-g) was examined. Extracellular activity was recorded from single WDR neurons that responded to noxious and innocuous stimuli applied to the cutaneous receptive field on the foot pads of the left hind paw. Results: After ipsilateral BK administration, the activity of the WDR neurons was found to be increased (excited) in all ten neurons that were examined. In contrast, the activity of these neurons was found to be decreased (inhibited) in five of these ten neurons after BK administration into the contralateral femoral artery. The 10 mg cntdot kg-1 dose of ketamine significantly suppressed the excitatory activity observed in all 15 of the WDR neurons examined. A comparison of the effects produced by the 0.5 mg cntdot kg-1 and the 10-mg cntdot kg-1 **intravenous** doses reveals that the amount of suppression was dose-related. In addition, the inhibitory WDR neuronal activity induced by contralateral BK injection was also significantly reduced by both the 0.5- and the 10-mg cntdot kg-1 doses of ketamide. Conclusions: These results indicate that this reduction of excitatory and inhibitory responses of WDR neurons after noxious stimulation is likely to be the fundamental basis for the spinal cord component of ketamine-induced analgesia.

L7 ANSWER 178 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1993:302357 BIOSIS
DN PREV199396020582
TI Modification of the renal response to endopeptidase inhibition and atrial natriuretic peptide infusion in normal dogs.
AU Levy, Mortimer (1); Cernacek, Peter
CS (1) Dep. Physiol., McGill Univ., 3655 Drummond St., Rm. 1228, Montreal,

Que. H3G 1Y6 Canada
SO Canadian Journal [redacted] Physiology and Pharmacology, ([redacted]92) Vol. 70, No. 12, pp. 1563-1570.
ISSN: 0008-4212.
DT Article
LA English
SL English; French
AB Inhibition of intrarenal neutral endopeptidase 24:11 (NEP) increases the natriuretic response in infused atrial natriuretic peptide (ANP). In various models of canine heart failure, angiotensin and kinins have been shown to modulate ANP and (or) NEP activity. In the present study, we examined possible modulators of NEP activity in normal dogs by infusing various agents into the left renal artery (or by denervating the left kidney) and comparing the response of this kidney with that of the contralateral one following the combined **intravenous** infusion of Squibb 28603 (a potent NEP inhibitor) and ANP (75 ng cntdot kg-1 cntdot min-1). Four dogs received angiotensin (1.5 ng cntdot kg-1 cntdot min-1) into the left renal artery, 8 dogs received saralasin (5 mu-g/min), 5 dogs received noradrenaline (2 mu-g/min), and 6 dogs received **bradykinin** (3 mu-g/min). Five dogs underwent left renall denervation. Angiotensin inhibited sodium excretion following the NEP inhibitor alone and after the NEP inhibitor plus ANP. Saralasin augmented the natriuretic response. None of the other protocols influenced sodium excretion. We conclude that angiotensin may modulate either the enzymatic degradation of ANP or influence its renal tubular effects.

L7 ANSWER 176 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1993:348956 BIOSIS
DN PREV199396045956
TI Role of peptidases and NK-1 receptors in vascular extravasation induced by
bradykinin in rat nasal mucosa.
AU Bertrand, Claude; Geppetti, Pierangelo; Baker, Jonathan; Petersson, Goran;
Piedimonte, Giovanni; Nadel, Jay A. (1)
CS (1) Cardioivascular Res. Inst., Box 0130, Univ. California, San Francisco,
CA 94143-0130 USA
SO Journal of Applied Physiology, (1993) Vol. 74, No. 5, pp. 2456-2461.
ISSN: 8750-7587.
DT Article
LA English
AB We used Evans blue dye to assess the effects of **bradykinin** on vascular extravasation in nasal mucosa of pathogen-free F344 rats. There was a dose-dependent increase in Evans blue extravasation when **bradykinin** was delivered by topical instillation in the nose (doses, 25-100 nmol). Only the highest **intravenous** doses (2 and 5 mu-mol/kg) of **bradykinin** caused increased extravasation. When **bradykinin** was delivered by either route, its effect on extravasation was exaggerated by pharmacological inhibition of the enzymes neutral endopeptidase (NEP) and kininase II (angiotensin-converting enzyme (ACE)). When **bradykinin** was instilled locally, the effect of NEP inhibition was predominant; when **bradykinin** was injected intravenously, the effect of ACE inhibition was predominant. The mechanism of extravasation also varied with the mode of **bradykinin** delivery: when **bradykinin** was instilled locally in the nose, the selective neurokinin-1 (NK-1) receptor antagonist CP-96,345 markedly inhibited the response, whereas it had no effect on Evans blue extravasation when **bradykinin** was injected intravenously. We conclude that **bradykinin** causes dose-related increases in Evans blue dye extravasation in the nose and that these effects are exaggerated when NEP and ACE are inhibited. Topically instilled **bradykinin** causes vascular extravasation to a large extent via NK-1 receptor stimulation, thus suggesting a major role for tachykinins released from sensory nerve endings.

L7 ANSWER 154 OF 269 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1994:278397 BIOSIS
DN PREV199497291397
TI **Bradykinin**-induced airway inflammation: Contribution of sensory neuropeptides differs according to airway site.
AU Nakajima, Natsuko; Ichinose, Masakazu; Takahashi, Tsuneyuki; Yamauchi, Hideyuki; Igarashi, Atsushi; Miura, Motohiko; Inoue, Hiroshi; Takishima, Tamotsu; Shirato, Kunio (1)
CS (1) First Dep. Intern. Med., Tohoku Univ. Sch. Med., 1-1 Seiryo-machi, Aoba-ku, Sendai 980 Japan
SO American Journal of Respiratory and Critical Care Medicine, (1994) Vol. 149, No. 3 PART 1, pp. 694-698.
DT Article
LA English
AB We examined the mechanisms of **bradykinin**-induced airway microvascular leakage in guinea pig airways by measuring extravasation of Evans blue dye. Animals were pretreated with propranolol (1 mg/kg, **intravenous**) and atropine (1 mg/kg, **intravenous**) to block the beta-adrenergic and muscarinic responses, respectively. **Bradykinin** (250 nmol) instillation into airways significantly increased the leakage of dye in the trachea, main bronchi, and intrapulmonary airways to the same degree. The **bradykinin** B-2-receptor antagonist HOE140 (500 nmol/kg, **intravenous**) did not alter basal leakage but almost completely inhibited **bradykinin** -mediated leakage. By contrast, the neurokinin NK-1 antagonist FK888 (10 mg/kg, **intravenous**) partially inhibited **bradykinin** -induced leakage in trachea (p lt 0.01) and main bronchi (p lt 0.01), but had no significant effect on intrapulmonary airways. Indomethacin (5 mg/kg, **intravenous**) had no effect on the plasma leakage after instilled **bradykinin**. We concluded that the airway inflammatory response to **bradykinin** administered directly into the airways is mediated by **bradykinin** B-2 receptors and partially mediated by tachykinin release from sensory nerve terminals, whereas cyclooxygenase products have no important role in the response. In the central airways, the contribution of sensory neuropeptides to the **bradykinin** response is greater than that caused by direct stimulation of the B-2 receptor on the endothelium at the postcapillary venule of the bronchial circulation. In contrast, in the peripheral airways, the contribution of direct B-2-receptor stimulation on the airway vasculature is greater than that involving sensory neuropeptides.

L

ANSWER 1015 OF 2045 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1994:79826 BIOSIS

DN PREV199497092826

TI Induction of **bradykinin** B-1 receptors in **vivo** in a model of ultra-violet irradiation-induced thermal hyperalgesia in the rat.

AU Perkins, M. N. (1); Kelly, D.

CS (1) Sandoz Inst. Med. Res., Gower Place, London EC1E 6BN UK

SO British Journal of Pharmacology, (1993) Vol. 110, No. 4, pp. 1441-1444. ISSN: 0007-1188.

DT Article

LA English

AB 1. The role of **bradykinin** B-1 receptors in the thermal hyperalgesia following unilateral ultra-violet (u.v.) irradiation of the hindpaw of rats has been investigated. 2. In non-irradiated (naive) animals the B-1 receptor agonist des-Arg-9-**bradykinin** and **bradykinin** (BK) (up to 1 mu-mol kg-1 i.v.) had no effect on withdrawal latency to a noxious heat stimulus when administered 60 min before testing. 3. Following exposure of one hindpaw to strong u.v. irradiation the withdrawal latency of the u.v.-treated paw to radiant noxious heat fell by a maximum of 50% after 48 h. There was no reduction in latency in the contralateral paw. 4. des-Arg-9-BK (1-100 nmol kg-1 i.v.) administered 24 h after u.v. exposure caused a further dose-dependent fall (50 +- 4% reduction from saline injected animals at 100 nmol kg-1 i.v.) in withdrawal latency in the u.v.-treated paw when measured 60 min after injection. The withdrawal latency of the contralateral paw was also reduced but to a lesser extent following des-Arg-9-BK (100 nmol kg-1 i.v.) with a maximum reduction of 19 +- 3%. 5. **Bradykinin** also induced a further reduction in withdrawal latency (33 +- 5% reduction at 1 mu-mol kg-1) although it was not as effective as des-Arg-9-BK. **Bradykinin** did not reduce the withdrawal latency in the contralateral paw. 6. The hyperalgesic action of both des-Arg-9-BK (10 nmol kg-1 i.v.) and **bradykinin** (100 nmol kg-1 i.v.) were antagonized by the B-1 receptor antagonist, des-Arg-9,Leu-8-BK (200 nmol kg-1 i.v.) but not by the B-2 receptor antagonist, HOE 140 (0.5 mu-mol kg-1 i.v.). 7. The results suggest that in conditions of inflammatory hyperalgesia **bradykinin** B-1 receptors are induced both locally and distant to the inflamed area, activation of which leads to further thermal hyperalgesia. In addition, in these conditions **bradykinin** appears to act predominantly via B-1 receptors, presumably after degradation to des-Arg-9-BK.

Bradykinin mw 1060

0.8

$$\frac{1\ \text{nmol}}{\text{Kg}} \times \frac{1060\ \text{ng}}{1\ \text{nmol}} = \frac{1060\ \text{ng}}{1\ \text{Kg}} = 1\ \mu\text{g/Kg}$$

N 2000080746 MEDLINE
DN 20080746
TI **Peptides** crossing the **blood-brain barrier**: some unusual observations.
AU Kastin A J; Pan W; Maness L M; Banks W A
CS VA Medical Center and Tulane University School of Medicine, 1601 Perdido Street, New Orleans, LA 70112-1262, USA.
NC DK54880 (NIDDK)
SO BRAIN RESEARCH, (1999 Nov 27) 848 (1-2) 96-100. Ref: 58
Journal code: B5L. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200005
EW 20000501
AB An interactive **blood-brain barrier** (BBB) helps regulate the passage of **peptides** from the periphery to the CNS and from the CNS to the periphery. Many **peptides** cross the BBB by simple diffusion, mainly explained by their lipophilicity and other physicochemical properties. Other **peptides** cross by saturable transport systems. The systems that transport **peptides** into or out of the CNS can be highly specific, transporting MIF-1 but not Tyr-MIF-1, PACAP38 but not PACAP27, IL-1 but not IL-2, and leptin but not the smaller ingestive **peptides** NPY, orexin A, orexin B, CART (55-102[Met(O)(67)]), MCH, or AgRP(83-132). Although the **peptides** EGF and TGF-alpha bind to the same receptor, only EGF enters by a rapid saturable transport system, suggesting that receptors and transporters can represent different proteins. Even the polypeptide NGF enters faster than its much smaller subunit beta-NGF. The saturable transport of some compounds can be upregulated, like TNF-alpha in EAE (an animal model of multiple sclerosis) and after spinal cord injury, emphasizing the regulatory role of the BBB. As has been shown for CRH, saturable transport from brain to blood can exert effects in the periphery. Thus, the BBB plays a dynamic role in the communication of **peptides** between the periphery and the CNS.

ANSWER 125 OF 143 MEDLINE

AN 83218159 MEDLINE

DN 83218159

TI Minireview. **Peptides** and the **blood-brain barrier**.

AU Meisenberg G; Simmons W H

SO LIFE SCIENCES, (1983 Jun 6) 32 (23) 2611-23. Ref: 140
Journal code: L62. ISSN: 0024-3205.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LA English

FS Priority Journals; Cancer Journals

EM 198309

AB Most neuropeptides are known to occur both in the central nervous system and in blood. This, as well as the occurrence of central nervous **peptide** effects after peripheral administration, show the importance of studying the relationships between the **peptides** in the two compartments. For many **peptides**, such as the enkephalins, TRH, somatostatin and MIF-1, poor penetration of the **blood-brain barrier** was shown. In other cases, including beta-endorphin and angiotensin, **peptides** are rapidly degraded during or just after their entry into brain or cerebrospinal fluid. Some **peptides**, such as insulin, delta-sleep-inducing **peptide**, and the lipotropin-derived **peptides**, enter the cerebrospinal fluid to a slight or moderate extent in the intact form. Many **peptide** hormones, such as insulin, calcitonin and angiotensin, act directly on receptors in the circumventricular organs, where the **blood-brain barrier** is absent. Oxytocin, vasopressin, MSH, and an MSH-analog alter the properties of the **blood-brain barrier**, which may result in altered nutritient supply to the brain. In conclusion, the diffusion of most **peptides** across the brain vascular endothelium seems to be severely restricted. There are, however, several alternative routes for peripheral **peptides** to act on the central nervous system. The **blood-brain barrier** is a major obstacle for the development of pharmaceutically useful **peptides**, as in the case of synthetic enkephalin-analogs.

L5 ANSWER 49 OF 143 MEDLINE
AN 95307461 MEDLINE
DN 95307461
TI Kinins and kinin receptors in the nervous system.
AU Walker K; Perkins M; Dray A
CS Sandoz Institute for Medical Research, London, U.K.
SO NEUROCHEMISTRY INTERNATIONAL, (1995 Jan) 26 (1) 1-16; discussion 17-26.
Ref: 180
Journal code: BNU. ISSN: 0197-0186.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199509
AB Kinins, including bradykinin and kallidin, are **peptides** that are produced and act at the site of tissue injury or inflammation. They induce a variety of effects via the activation of specific B1 or B2 receptors that are coupled to a number of biochemical transduction mechanisms. In the periphery the actions of kinins include vasodilatation, increased vascular permeability and the stimulation of immune cells and **peptide**-containing sensory neurones to induce pain and a number of neuropeptide-induced reflexes. Mechanisms for kinin synthesis are also present in the CNS where kinins are likely to initiate a similar cascade of events, including an increase in blood flow and plasma leakage. Kinins are potent stimulators of neural and neuroglial tissues to induce the synthesis and release of other pro-inflammatory mediators such as prostanoids and cytotoxins (cytokines, free radicals, nitric oxide). These events lead to neural tissue damage as well as long lasting disturbances in **blood-brain barrier** function. Animal models for CNS trauma and ischaemia show that increases in kinin activity can be reversed either by kinin receptor antagonists or by the inhibition of kinin production. A number of other central actions have been attributed to kinins including an effect on pain signalling, both within the brain (which may be related to vascular headache) and within the spinal dorsal horn where primary afferent nociceptors can be stimulated. Kinins also appear to play a role in cardiovascular regulation especially during chronic spontaneous hypertension. Presently, however, direct evidence is lacking for the release of kinins in pathophysiological conditions of the CNS and it is not known whether spinal or central neurones, other than afferent nerve terminals, are sensitive to kinins. A more detailed examination of the effects of kinins and their central pharmacology is necessary. It is also important to determine whether the inhibition of kinin activity will alleviate CNS inflammation and whether kinin receptor antagonists are useful in pathological conditions of the CNS.

5 ANSWER 34 OF 143 MEDLINE
AN 97120478 MEDLINE
DN 97120478
TI How structural features influence the biomembrane permeability of **peptides**.
AU Burton P S; Conradi R A; Ho N F; Hilgers A R; Borchardt R T
CS Drug Delivery Systems Research, Pharmacia and Upjohn, Inc., Kalamazoo, MI 49001, USA.
SO JOURNAL OF PHARMACEUTICAL SCIENCES, (1996 Dec) 85 (12) 1336-40. Ref: 55
Journal code: JO7. ISSN: 0022-3549.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199705
EW 19970502
AB Successful drug development requires not only optimization of specific and potent pharmacological activity at the target site, but also efficient delivery to that site. Many promising new **peptides** with novel therapeutic potential for the treatment of AIDS, cardiovascular diseases, and CNS disorders have been identified, yet their clinical utility has been limited by delivery problems. Along with metabolism, a major factor contributing to the poor bioavailability of **peptides** is thought to be inefficient transport across cell membranes. At the present time, the reasons for this poor transport are poorly understood. To explore this problem, we have designed experiments focused on determining the relationship between **peptide** structure and **peptide** transport across various biological membranes both in vitro and in vivo. Briefly, **peptides** that varied systematically in chain length, lipophilicity, and amide bond number were prepared. Permeability results with these solutes support a model in which the principal determinant of **peptide** transport is the energy required to desolvate the polar amides in the **peptide** for the **peptide** to enter and diffuse across the cell membrane. Further impacting on **peptide** permeability is the presence of active, secretory transport systems present in the apical membrane of intestinal epithelial and brain endothelial cells. In Caco-2 cell monolayers, a model of the human intestinal mucosa, this pathway displayed substrate specificity, saturation, and inhibition. Similar results have been shown in vivo in both rat intestinal and **blood-brain barrier** absorption models. The presence of such systems serves as an additional transport barrier by returning a fraction of absorbed **peptide** back to the lumen.

L5 ANSWER 36 OF 143 MEDLINE
AN 97089253 MEDLINE
DN 97089253
TI The **blood-brain barrier**: principles for targeting **peptides** and drugs to the central nervous system.
AU Begley D J
CS Biomedical Sciences Division, King's College London, UK.
SO JOURNAL OF PHARMACY AND PHARMACOLOGY, (1996 Feb) 48 (2) 136-46. Ref: 47
Journal code: JNR. ISSN: 0022-3573.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199703
EW 19970301
AB The presence of the **blood-brain barrier** (BBB), reduces the brain uptake of many drugs, **peptides** and other solutes from blood. Strategies for increasing the uptake of drugs and **peptide**-based drugs include; structural modifications to increase plasma half-life; improving passive penetration of the BBB by increasing the lipophilicity of the molecule; designing drugs which react with transporters present in the BBB; and reducing turnover and efflux from the central nervous system (CNS).

AN 1998054557 MEDLINE
DN 98054557
TI Bioavailability and transport of **peptides** and **peptide** drugs into the brain.
AU Egleton R D; Davis T P
CS Department of Pharmacology, University of Arizona College of Medicine, Tucson 85724, USA.
SO PEPTIDES, (1997) 18 (9) 1431-9. Ref: 85
Journal code: PA7. ISSN: 0196-9781.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199803
EW 19980305
AB Rational drug design and the targeting of specific organs has become a reality in modern drug development, with the emergence of molecular biology and receptor chemistry as powerful tools for the pharmacologist. A greater understanding of **peptide** function as one of the major extracellular message systems has made neuropeptides an important target in neuropharmaceutical drug design. The major obstacle to targeting the brain with therapeutics is the presence of the **blood-brain barrier** (BBB), which controls the concentration and entry of solutes into the central nervous system. **Peptides** are generally polar in nature, do not easily cross the **blood-brain barrier** by diffusion, and except for a small number do not have specific transport systems. **Peptides** can also undergo metabolic deactivation by peptidases of the blood, brain and the endothelial cells that comprise the BBB. In this review, we discuss a number of the recent strategies which have been used to promote **peptide** stability and **peptide** entry into the brain. In addition, we approach the subject of targeting specific transport systems that can be found on the brain endothelial cells, and describe the limitations of the methodologies that are currently used to study brain entry of neuropharmaceuticals.

SWER 22 OF 143 MEDLINE
AN 1998231972 MEDLINE
DN 98231972
TI CNS drug design based on principles of **blood-brain barrier** transport.
AU Pardridge W M
CS Department of Medicine, Brain Research Institute, UCLA School of Medicine,
Los Angeles, California 90095-1682, USA.
NC NS34698 (NINDS)
SO JOURNAL OF NEUROCHEMISTRY, (1998 May) 70 (5) 1781-92. Ref: 98
Journal code: JAV. ISSN: 0022-3042.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199807
EW 19980704
AB Lipid-soluble small molecules with a molecular mass under a 400-600-Da threshold are transported readily through the **blood-brain barrier** in vivo owing to lipid-mediated transport. However, other small molecules lacking these particular molecular properties, antisense drugs, and **peptide**-based pharmaceuticals generally undergo negligible transport through the **blood-brain barrier** in pharmacologically significant amounts. Therefore, if present day CNS drug discovery programs are to avoid termination caused by negligible **blood-brain barrier** transport, it is important to merge CNS drug discovery and CNS drug delivery as early as possible in the overall CNS drug development process. Strategies for special formulation that enable drug transport through the **blood-brain barrier** arise from knowledge of the molecular and cellular biology of **blood-brain barrier** transport processes.

=> d bib ab 1-39

L11 ANSWER 1 OF 39 MEDLINE
AN 2000216092 MEDLINE
DN 20216092
TI Pharmacokinetics of carboplatin **administered** in combination with the **bradykinin** agonist Cereport (RMP-7) for the treatment of brain tumours.
AU Thomas H D; Lind M J; Ford J; Bleehen N; Calvert A H; Boddy A V
CS Cancer Research Unit, Medical School, University of Newcastle upon Tyne, UK.
SO CANCER CHEMOTHERAPY AND PHARMACOLOGY, (2000) 45 (4) 284-90.
Journal code: C9S. ISSN: 0344-5704.
CY GERMANY: Germany, Federal Republic of
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 200006
EW 20000604
AB INTRODUCTION: Cereport (RMP-7) is a novel bradykinin agonist which is being developed as a modulator of the blood-brain barrier (BBB). In order to investigate the pharmacokinetics of carboplatin in combination with Cereport, we performed pharmacological studies in conjunction with early clinical trials. METHODS: Pharmacokinetic samples were collected from eight patients in a phase I study (Cereport 100-300 ng/ kg) and ten patients in a phase II study (Cereport 300 ng/kg). Pharmacokinetic parameters for carboplatin were compared with respect to the dose of Cereport and with historical controls. RESULTS: Cereport combined with carboplatin was well-tolerated, with mild haematological toxicities consistent with the target area under the concentration time curve (AUC) of 7 mg/ml x min. Although the clearance of carboplatin was within the range reported for this drug alone, the addition of Cereport resulted in a higher than expected carboplatin AUC. This effect was related to the dose of Cereport in the phase I study (AUC values 104-133% of target, Spearman rank correlation coefficient = 0.71, $P < 0.001$). The higher than expected AUC value was confirmed in the phase II study (AUC values 106-189% of target). CONCLUSIONS: Co-administration of Cereport with carboplatin may result in a greater than predicted AUC. The mechanism of this possible interaction remains to be determined, although this did not result in any increased toxicity. Thus, the clinical potential of this combination in the treatment of brain tumours warrants further investigation.

L11 ANSWER 2 OF 39 MEDLINE
AN 1998420984 MEDLINE
DN 98420984
TI [Effect of chronic **bradykinin** infusion on angiotensin II hypertension in rats].
Effet de l'**administration** chronique de bradykinine dans l'hypertension induite par l'angiotensine II chez le rat.
AU Pasquie J L; Herizi A; Jover B; du Cailar G; Mimran A
CS Groupe rein et hypertension, Institut universitaire de recherche clinique,
Montpellier.

SO ARCHIVES DES MALADIES DU COEUR ET DES VAISSEAUX, (1998 Aug) 91 (8) 1035-8.
Journal code: 7SM. ISSN: 0003-9683.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals
EM 199812
EW 19981202
AB In previous studies, we demonstrated that in ANG II-treated rats, prevention of cardiac hypertrophy (CH) by enalapril was blunted by bradykinin (BK) blockade by Hoe140. The putative role of BK was assessed by chronic exogenous BK infusion and in 46 male Sprague-Dawley rats infused with ANG II. ANG II (200 ng/kg/min) alone and associated with BK at low (BKlow, 15 ng/kg/day), mid (BKmid, 100 ng/kg/day) and high doses (BKhigh, 100 ng/kg/min) were delivered by Alzet osmotic pumps for 10 days and compared to control animals (Veh). Values of systolic arterial pressure (SAP, mmHg) in conscious rats and heart weight (HW, mg/g bw) at the end of the study are reported below. Results were submitted to ANOVA and are expressed as mean +/- SEM.

L11 ANSWER 3 OF 39 MEDLINE
AN 1998355856 MEDLINE
DN 98355856
TI Effect of chronic **bradykinin administration** on insulin action in an animal model of insulin resistance.
AU Henriksen E J; Jacob S; Fogt D L; Dietze G J
CS Muscle Metabolism Laboratory, Department of Physiology, University of Arizona College of Medicine, Tucson, Arizona 85721-0093, USA.
SO AMERICAN JOURNAL OF PHYSIOLOGY, (1998 Jul) 275 (1 Pt 2) R40-5.
Journal code: 3U8. ISSN: 0002-9513.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199810
EW 19981005
AB The nonapeptide bradykinin (BK) has been implicated as the mediator of the beneficial effect of angiotensin-converting enzyme inhibitors on insulin-stimulated glucose transport in insulin-resistant skeletal muscle.
In the present study, the effects of chronic in vivo BK treatment of obese Zucker (fa/fa) rats, a model of glucose intolerance and severe insulin resistance, on whole body glucose tolerance and skeletal muscle glucose transport activity stimulated by insulin or contractions were investigated. BK was administered subcutaneously (twice daily at 40 microg/kg body wt) for 14 consecutive days. Compared with a saline-treated obese group, the BK-treated obese animals had significantly ($P < 0.05$) lower fasting plasma levels of insulin (20%) and free fatty acids (26%), whereas plasma glucose was not different. During a 1 g/kg body wt oral glucose tolerance test, the glucose and insulin responses [incremental areas under the curve (AUC)] were 21 and 29% lower, respectively, in the BK-treated obese group. The glucose-insulin index, the product of the glucose and insulin AUCs and an indirect index of in vivo insulin action, was 52% lower in the BK-treated obese group compared with the obese control group. Moreover, 2-deoxyglucose uptake in the isolated epitrochlearis muscle stimulated by a maximally effective dose of insulin (2 mU/ml) was 52% greater in the BK-treated obese group. Contraction-stimulated (10 tetani) 2-deoxyglucose uptake was also enhanced by 35% as a result of the BK treatment. In conclusion, these findings indicate that in the severely insulin-resistant obese Zucker rat, chronic

in vivo treatment with BK can significantly improve whole body glucose tolerance, possib[redacted] as a result of the enhanced in[redacted]lin-stimulated skeletal muscle gl[redacted]cose transport activity observe[redacted]n these animals.

L11 ANSWER 4 OF 39 MEDLINE
AN 97422053 MEDLINE
DN 97422053
TI Oral activity of peptide **bradykinin** antagonists following intragastric **administration** in the rat.
AU Whalley E T; Hanson W L; Stewart J M; Gera L
CS Cortech Inc., Denver, CO 80221, USA.
SO CANADIAN JOURNAL OF PHYSIOLOGY AND PHARMACOLOGY, (1997 Jun) 75 (6) 629-32.
Journal code: CJM. ISSN: 0008-4212.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
EW 19980104
AB This study has investigated the oral activity, following intragastric administration, of three potent and long-acting peptide-based bradykinin antagonists, HOE-140, B9430, and CP-0597, in the anesthetized rat, using bradykinin-induced hypotension. Two of the three bradykinin antagonists, B9430 and HOE-140, but not CP-0597, were found to be active following intragastric administration, producing dose-dependent (1, 3, and 10 mg/kg) and selective inhibition of bradykinin-induced hypotension. At a dose of 10 mg/kg, the inhibition of bradykinin-induced hypotension occurred within 15 min and lasted for at least 2 h, which was the duration of the experiment. HOE-140 and CP-0597, 10 micrograms/kg i.v., produced significant inhibition of bradykinin-induced responses that lasted for 60 min. B9430, 10 micrograms/kg i.v., produced a significantly greater inhibition than HOE-140 and CP-0597, this inhibition being significant for the duration of the experiment (2 h) compared with saline controls. Considering the close chemical structure of CP-0597 compared with HOE-140 and B9430, it is not clear as to why CP-0597 was inactive via the intragastric route. This is the first demonstration of the oral activity of peptide-based bradykinin antagonists following intragastric administration in the rat.

L11 ANSWER 5 OF 39 MEDLINE
AN 97053442 MEDLINE
DN 97053442
TI Repeated cocaine **administration** reduces **bradykinin** -induced dilation of pial arterioles.
AU Copeland J R; Willoughby K A; Police R J; Ellis E F
CS Department of Pharmacology and Toxicology, Medical College of Virginia, Virginia Commonwealth University, Richmond 23298-0613, USA.
NC DA-05274 (NIDA)
NS-07288 (NINDS)
SO AMERICAN JOURNAL OF PHYSIOLOGY, (1996 Oct) 271 (4 Pt 2) H1576-83.
Journal code: 3U8. ISSN: 0002-9513.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
AB Using the acute cranial window technique in rabbits under surgical anesthesia, we tested the vasoactivity of acetylcholine (ACh, 10(-8)-10(-5) M), bradykinin (BK, 10(-8)-10(-5) M), and asphyxia (10% O2, 9% CO2, balance N2) after subchronic pretreatment with cocaine. After repeated administration of cocaine (20 mg.kg-1.day-1 sc x 7 days), the

BK-induced dilation of pial arterioles was reduced by 51%. Previous work showed that BK pr[redacted]ces dilation of pial arteriole[redacted]by a cyclooxygenase-de[redacted]dent oxygen radical-mediated m[redacted]anism and that in rabbits the BK-induced dilation is dependent on both vascular and nonvascular cyclooxygenase. Selective blockade of vascular cyclooxygenase, in addition to cocaine treatment, did not produce any greater inhibition of the BK-induced dilation. The dilation in response to ACh and asphyxia was unaltered by cocaine. Levels of cerebrospinal fluid prostaglandins suggest cocaine pretreatment may inhibit cerebral vascular prostaglandin production. Together, cerebrospinal fluid prostaglandin and vasoreactivity data indicate cocaine pretreatment selectively inhibits the vascular cyclooxygenase-dependent mechanism mediating the BK-induced dilation. This decreased response to BK in cocaine-treated rabbits may result from decreased oxygen radical production concomitant with decreased vascular prostaglandin production. Alternatively, oxygen radical scavenging may be increased after cocaine treatment. We speculate that cocaine-induced alterations in cerebrovascular function and metabolism may be related to the increased incidence of stroke reported to occur in human cocaine users.

L11 ANSWER 6 OF 39 MEDLINE
AN 96436938 MEDLINE
DN 96436938
TI Effects of the prolonged **administration** of **bradykinin** on the rat pituitary-adrenocortical axis.
AU Malendowicz L K; Macchi C; Nussdorfer G G; Markowska A
CS Department of Histology and Embryology, School of Medicine, Poznan, Poland.
SO HISTOLOGY AND HISTOPATHOLOGY, (1996 Jul) 11 (3) 641-5.
Journal code: BEM. ISSN: 0213-3911.
CY Spain
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199704
EW 19970404
AB The effects of a prolonged administration of bradykinin (BK) and/or D-Arg, [Hyp3, D-Phe7]-BK, a specific antagonist of BK receptors (BK-A) (daily subcutaneous injections of 4 nmol/rat for 6 days) on the function of the pituitary-adrenocortical axis were investigated. BK did not change plasma aldosterone concentration (PAC), but markedly lowered that of corticosterone (PBC) and consequently induced a compensatory hypersecretion of ACTH by the pituitary gland. BK-A did not apparently affect the function and growth of the adrenal gland, but, when administered together with BK, markedly raised both PAC and PBC, and provoked a significant atrophy of the adrenal gland, probably due to loss of parenchymal cells. Taken together, these rather puzzling findings do not appear to provide clear evidence for the involvement of BK in the physiological regulation of adrenocortical growth and steroidogenic capacity in rats.

L11 ANSWER 7 OF 39 MEDLINE
AN 96423909 MEDLINE
DN 96423909
TI Hyperalgesia in rats following intracerebroventricular **administration** of endotoxin: effect of **bradykinin** B1 and B2 receptor antagonist treatment.
AU Walker K; Dray A; Perkins M
CS Sandoz Institute for Medical Research, London, UK.
SO PAIN, (1996 May-Jun) 65 (2-3) 211-9.
Journal code: OPF. ISSN: 0304-3959.

CY Netherlands
DT Journal; Article; OURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
EW 19970503
AB The present study investigated the development of thermal and mechanical hyperalgesia following intracerebroventricular (i.c.v.) injections of E. coli lipopolysaccharide (LPS). Hind paw withdrawal to von Frey filament stimulation and thermal withdrawal latencies were measured before and up to 24 or 48 h following an i.c.v. injection of LPS (dose range: 0.02--200 micrograms). Thermal and mechanical hyperalgesia were evident by 6 h after LPS injection. LPS-induced hyperalgesia was reversed by the B2 receptor antagonist, HOE 140 (10--30 pmol), when administered i.c.v. but not systemically (0.01--1 mmol/kg, i.v.). Central co-administration of the B1 receptor antagonists, des-Arg9-Leu8 Bk (0.1--1 nmol) or des-Arg10 HOE 140 (0.1--1 nmol) had no effect on thermal or mechanical hyperalgesia. LPS-induced hyperalgesia was also inhibited by indomethacin administered either i.c.v. (10 nmol) or i.v. (1 mumol/kg). These results indicate that administration of endotoxin to the CNS induces the development of hyperalgesia and that this response involves the activity of kinins, via the stimulation of centrally located B2 receptors, and the formation of prostanoids.

L11 ANSWER 8 OF 39 MEDLINE
AN 96326854 MEDLINE
DN 96326854
TI Role of tachykinins in bronchoconstriction induced by intravenous **administration** of **bradykinin** in guinea-pigs.
AU Kuroiwa C; Umeno E; Nogami H; Kano S; Hirose T; Nishima S
CS Clinical Research Institute, National Minami Fukuoka Chest Hospital, Fukuoka, Japan.
SO EUROPEAN RESPIRATORY JOURNAL, (1996 Apr) 9 (4) 741-6.
Journal code: ERY. ISSN: 0903-1936.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199701
EW 19970104
AB To elucidate the role of tachykinins in bronchoconstriction induced by intravenous administration of bradykinin (Bk), we studied the effects of FK224, a neurokinin-1 (NK1) and neurokinin-2 (NK2) receptor antagonist, on the bronchoconstriction induced by intravenous (i.v.) administration of Bk (5-100 micrograms.kg-1) in guinea-pigs. Total pulmonary resistance -(RL) was measured using a pressure-volume sensitive body plethysmograph in anaesthetized artificially ventilated guinea-pigs pretreated with atropine (1 mg.kg-1) and propranolol (1 mg.kg-1). In the control group, i.v. administration of Bk produced a dose-dependent increase in RL. In animals pretreated with FK224, bronchoconstriction induced by higher doses of Bk (10, 50 and 100 micrograms.kg-1) was significantly reduced, whilst the bronchoconstriction caused by lower doses of Bk (5 and 7.5 micrograms.kg-1) was not. Pretreatment with a combination of FK224 and indomethacin markedly inhibited the bronchoconstriction induced by each dose of Bk compared with the groups pretreated with FK224 alone. Although pretreatment with indomethacin alone significantly reduced RL at a high dose of Bk (50 micrograms.kg-1), the reduction was significantly lower than that produced by a combination of FK224 and indomethacin. These results suggest that intravenous administration of a high dose of bradykinin causes bronchoconstriction both by cyclo-oxygenase products and

by release of tachykinins.

L11 ANSWER 9 OF 39 MEDLINE
AN 96098838 MEDLINE
DN 96098838
TI [The neuronal reaction of the sensorimotor cortex to stimulation of the lateral hypothalamus with a background of the microiontophoretic **administration** of tetragastrin and **bradykinin**: the role of food reinforcement].
Reaktsiia neironov sensomotornoi kory na razdrazhenie lateral'nogo gipotalamusa na fone mikroionoforeticheskogo podvedeniia tetragastrina i bradikinina: rol' pishchevogo podkrepleniia.
AU Kravtsov A N; Sudakov S K
SO ZHURNAL VYSSHEI NERVNOI DEIATELNOSTI IMENI I. P. PAVLOVA, (1995 Jul-Aug) 45 (4) 757-64.
Journal code: YAS. ISSN: 0044-4677.
CY RUSSIA: Russian Federation
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals
EM 199604
AB Reactions of neurons of sensorimotor cortex to stimulation of the "center of hunger" in the lateral hypothalamus were studied at the background of microiontophoretic application of gastrin, and bradikinin in satiated freely behaving rabbits under conditions of presence or absence of free access to food. It was shown that food reinforcement essentially changed reactions of neurons to electrical stimulation of the lateral hypothalamus at the background of application of neuropeptides under study. This probably led to specific reorganization in the neuronal system which underlay the mechanism of interaction between motivation and reinforcement influences on the neurons.

L11 ANSWER 10 OF 39 MEDLINE
AN 96013080 MEDLINE
DN 96013080
TI Use of an indwelling catheter for examining cardiovascular responses to pericardial **administration** of **bradykinin** in rat.
AU McDermott D A; Meller S T; Gebhart G F; Gutterman D D
CS Department of Internal Medicine, College of Medicine, University of Iowa, Iowa City 52242-1194, USA..
NC HL 32295 (NHLBI)
NS19912 (NINDS)
NS29844 (NINDS)
SO CARDIOVASCULAR RESEARCH, (1995 Jul) 30 (1) 39-46.
Journal code: COR. ISSN: 0008-6363.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199601
AB OBJECTIVE AND METHODS: Epicardial application of pharmacologic agonists has been used to study nociceptive and reflex responses to agents such as bradykinin. We utilized a model where intrapericardial bradykinin was administered in a closed-chest rat. The procedure allows for reproducible administration of microliter doses of pharmacologic agonists in both conscious and anesthetized animals. RESULTS: Bradykinin (BK) has been shown to produce sympathoexcitatory reflexes when applied to the heart. BK typically produced a dose-dependent (0.001-10 micrograms) decrease in arterial blood pressure and tachycardia in pentobarbital-anesthetized rats. In contrast, in alpha-chloralose-anesthetized or awake rats, pericardial administration of BK produced a dose-dependent (0.001-10 micrograms) increase in arterial blood pressure and tachycardia. Maximal

cardiovascular changes were produced by 1 microgram BK. The maximum change in arterial pressure was +33.6 +/- 9% in awake, +3[illegible]9 +/- 6% in chloralose-anesthetized, and -20 +/- 7% in pentobarbital-anesthetized rats. In alpha-chloralose-anesthetized rats, tachyphylaxis to pericardial administration of 1 microgram BK occurred at 5 and 15, but not at 30 min dosing intervals. Administration of the receptor selective B2-antagonist D-Arg,[Hyp3,Thi5,8 D-Phe7]-BK (200 micrograms) or the mixed B2/B1 antagonist [Thi5,8,D-Phe7]-BK (200 micrograms), produced similar attenuation of the pressor and tachycardia responses to BK. Bilateral transection of the cervical vagus nerve, bilateral removal of the stellate ganglion or ganglion blockade (hexamethonium), but not administration of indomethacin, reduced the magnitude of the tachycardia to BK. Only ganglionic blockade significantly reduced the pressor response to BK. CONCLUSIONS: These results demonstrate that pericardial administration of BK produces a tachycardia and pressor effect in awake and alpha-chloralose-anesthetized rats and a tachycardia and depressor effect in pentobarbital-anesthetized rats. These responses appear to be mediated through activation of BK (presumably B2) receptors on cardiac vagal and sympathetic afferents, and may include a direct action of BK on the heart. This model of pericardial administration of pharmacologic agonists may be useful in studies of cardiac pain and reflex responses.

L11 ANSWER 11 OF 39 MEDLINE
AN 95295014 MEDLINE
DN 95295014
TI **Bradykinin** receptor and tissue ACE binding in myocardial fibrosis: response to chronic angiotensin II or aldosterone **administration** in rats.
AU Sun Y; Ratajska A; Weber K T
CS Department of Internal Medicine, University of Missouri Health Sciences Center, Columbia, USA..
NC R01-HL-31701 (NHLBI)
SO JOURNAL OF MOLECULAR AND CELLULAR CARDIOLOGY, (1995 Feb) 27 (2) 813-22. Journal code: J72. ISSN: 0022-2828.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199509
AB High density angiotensin converting enzyme (ACE) binding is present in the perivascular fibrosis involving intramyocardial coronary arteries and the microscopic scarring of the myocardium that accompanies chronic elevations in circulating angiotensin II (AngII) and/or aldosterone (ALDO). As a kininase II, ACE degrades bradykinin. Herein we sought to determine whether bradykinin (BK) receptor binding was associated with ACE binding in each of these experimental models. BK receptor binding was localized and quantified by in vitro quantitative autoradiography, using [125I-Tyr8]BK. In serial sections of the same heart hematoxylin and eosin (H&E) and picrosirius red (PSR) staining were utilized to address cardiac myocyte injury and fibrosis, respectively. Four experimental groups were examined: unoperated, untreated, age/sex matched controls: age/sex matched uninephrectomized control rats receiving a high sodium diet; animals that received AngII (9 micrograms/h sc) for 2, 4 or 6 weeks; and uninephrectomized rats on a high sodium diet that received ALDO (0.75 micrograms/h sc) for similar periods of time. We found: (a) myocardial fibrosis, including perivascular fibrosis and microscopic scarring, at week 2 of AngII, but not until week 4 or more of ALDO treatment; (b) low BK receptor binding in normal ventricles that was increased in scars and markedly increased in perivascular fibrosis at week 2 of AngII and each

increased further at week 4 and 6 of AngII: (c) low BK receptor binding at week 2 and 4 weeks of ALDO treatment which became markedly increased at fibrous tissue sites at week 6. BK receptor and ACE binding were anatomically coincident and localized to each site of fibrosis in both models. The co-location of BK receptor and ACE binding in these models raises the prospect that fibrous tissue ACE may utilize BK as substrate and BK, in turn, may play a role in fibrous tissue formation.

L11 ANSWER 12 OF 39 MEDLINE
AN 94138646 MEDLINE
DN 94138646
TI Cardiovascular effects of intrathecally **administered** **bradykinin** in the rat: characterization of receptors with antagonists.
AU Lopes P; Regoli D; Couture R
CS Department of Physiology, Faculty of Medicine, Universite de Montreal, Quebec, Canada..
SO BRITISH JOURNAL OF PHARMACOLOGY, (1993 Dec) 110 (4) 1369-74.
Journal code: B00. ISSN: 0007-1188.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199405
AB 1. The effects of intrathecal (i.t.) pretreatment with selective B1 or B2 kinin receptor antagonists were studied on the cardiovascular response to i.t. injection of bradykinin (BK) in conscious freely moving rats. 2. BK (81 pmol) produced an increase in mean arterial pressure (MAP: 9-13 mmHg) and decrease in heart rate (HR: 20-30 beats min-1) that reached a maximum 2 min after injection. 3. The BK-induced cardiovascular responses were dose-dependently and reversibly reduced by four antagonists with the following rank order of potency: Tyr, D-Arg[Hyp3,D-Phe7,Leu8]-BK = D-Arg[Tyr3,D-Phe7,Leu8]-BK = D- Arg[Hyp3,D-Phe7,Leu8]-BK > D-Arg[Hyp3,Thi5,D-Tic7,Oic8]-BK (Hoe 140). These compounds failed to alter the cardiovascular response to i.t. injection of 8.1 nmol of substance P. 4. Other compounds acting on the B2 receptor, namely D-Arg[Hyp3,Gly6,Leu8]-BK, D-Arg[Hyp3,D-Phe7]-BK, D-Arg[Hyp2,Thi5,8,D-Phe7]-BK and D-Arg[Hyp3,Gly6,D-Phe7,Leu8]-BK or on the B1 receptor, [Leu8]-desArg9-BK, did not influence the cardiovascular responses to BK at doses devoid of intrinsic activity on MAP and HR. 5. None of the kinin receptor antagonists caused motor impairment, respiratory arrest or persisting cardiovascular changes. 6. These results confirm that the cardiovascular effects induced by i.t. BK are mediated by the activation of a B2 receptor in the rat spinal cord. However, the rank order of potency of antagonists does not conform to the classical B2 functional site characterized in peripheral tissues.

L11 ANSWER 13 OF 39 MEDLINE
AN 93140944 MEDLINE
DN 93140944
TI Chronically **administered** nicotine attenuates **bradykinin** -induced plasma extravasation and aggravates arthritis-induced joint injury in the rat.
AU Miao F J; Helms C; Benowitz N L; Basbaum A I; Heller P H; Levine J D
CS Department of Medicine, University of California, School of Medicine, San Francisco 94143-0452A.
NC NS-07265 (NINDS)
SO NEUROSCIENCE, (1992 Dec) 51 (3) 649-55.
Journal code: NZR. ISSN: 0306-4522.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 199304
AB We recently showed that acute administration of nicotine in the rat decreases bradykinin-induced plasma extravasation and that adrenal medullary-derived epinephrine, acting at a beta 2-adrenergic receptor, mediates the nicotine effect. Since agents which decrease bradykinin-induced plasma extravasation have been associated with increased joint injury in a rat model of chronic inflammation (experimental arthritis induced by subcutaneous injection of Mycobacterium butyricum) we examined the effect of chronic nicotine on both plasma extravasation and the severity of joint injury. In normal rats, bradykinin-induced plasma extravasation was decreased after nicotine administered both by repeated injection (10(-2) mg/kg, s.c., once per h for 4 h) and by continuous long-term infusion (subcutaneous mini-osmotic pump; 1.5 x 10(-3) mg/kg per h for 30 days). Nicotine-induced inhibition of bradykinin-induced plasma extravasation did not show tachyphylaxis. In rats with arthritis, chronic administration of nicotine also produced a decrease in bradykinin-induced plasma extravasation. This effect of chronic nicotine in the arthritic rats was antagonized by co-administration of hexamethonium (a nicotinic receptor antagonist), by surgical removal of the adrenal medulla, or by co-administration of ICI-118,551 (a beta 2-adrenoceptor antagonist). Chronic administration of nicotine decreased the latency to the onset of arthritis and, in a dose-dependent manner, led to an increase in the radiographic joint injury score.(ABSTRACT TRUNCATED AT 250 WORDS)

L11 ANSWER 14 OF 39 MEDLINE
AN 93047701 MEDLINE
DN 93047701
TI Responses of airway rapidly adapting receptors to **bradykinin** before and after **administration** of enalapril in rabbits.
AU Hargreaves M; Ravi K; Senaratne M P; Kappagoda C T
CS Division of Cardiology, University of Alberta, Edmonton, Canada..
SO CLINICAL SCIENCE, (1992 Oct) 83 (4) 399-407.
Journal code: DIZ. ISSN: 0143-5221.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199302
AB 1. The present study was performed in anaesthetized, artificially ventilated, open-chested rabbits to examine whether (a) the rapidly adapting receptors of the airways were stimulated by exogenously administered bradykinin, and (b) if this sensitivity could be enhanced by the angiotensin-converting-enzyme inhibitor, enalapril. 2. Rapidly adapting receptor activity (n = 8) was recorded from the cervical vagus. Bradykinin was injected intravenously (0.25-1.0 microgram/kg) and a dose-response curve relating receptor activity to bradykinin was elicited.
In the control state, the threshold dose of bradykinin required for stimulation of rapidly adapting receptors was 0.53 +/- 0.11 microgram/kg. Five minutes after the administration of enalapril maleate (2 mg intravenously), the dose-response curve was shifted to the left significantly ($P < 0.01$). 3. In seven other rapidly adapting receptors, enalapril (2 mg) increased the resting activity significantly ($P < 0.05$) over a period of 60 min. This increase was significantly different from the spontaneous variation in neural activity of rapidly adapting receptors (n = 7) recorded over a period of 60 min. 4. Bradykinin either alone (0.25-1.0 microgram/kg) or in the presence of enalapril did not stimulate the slowly adapting receptors (n = 5) of the airways. 5. These results show that (a) exogenous bradykinin stimulates the rapidly adapting

receptors, (b) the sensitivity of rapidly adapting receptors to bradykinin
is enhanced by enalapril and (c) enalapril increases the resting activity of rapidly adapting receptors. It is suggested that the cough reported after the administration of enalapril may be due to stimulation of rapidly
adapting receptors of the airways.

L11 ANSWER 15 OF 39 MEDLINE
AN 89016171 MEDLINE
DN 89016171
TI [Comparative study of the nociceptive reactions when **bradykinin** is **administered** in different receptor areas to waking animals]. Sravnitel'noe izuchenie notsitseptivnykh reaktsii pri vvedenii bradikinina
v raznye retseptornye zony bodrstvuiushchim zhivotnym.
AU Panov A V
SO PATOLOGICHESKAIA FIZIOLOGIIA I EKSPERIMENTALNAIA TERAPIIA, (1988 May-Jun) (3) 9-11.
Journal code: OTF. ISSN: 0031-2991.
CY USSR
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
EM 198901

L11 ANSWER 16 OF 39 MEDLINE
AN 88286372 MEDLINE
DN 88286372
TI Intracerebroventricularly **administered bradykinin** augments carrageenan-induced paw oedema in rats.
AU Bhattacharya S K; Mohan Rao P J; Das N; Das Gupta G
CS Department of Pharmacology, Banaras Hindu University, Varanasi, India..
SO JOURNAL OF PHARMACY AND PHARMACOLOGY, (1988 May) 40 (5) 367-9.
Journal code: JNR. ISSN: 0022-3573.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198811
AB Intracerebroventricular (i.c.v.) administered bradykinin (2.5 and 5.0 micrograms/rat) was found to augment carrageenan-induced acute paw oedema throughout the 4 h post-carrageenan observation period. The effect was statistically significant with the higher dose. The pro-inflammatory effect of i.c.v. bradykinin was antagonized following pretreatment with hemicholinium and atropine ethoiodide administered i.c.v., drugs that reduce central cholinergic activity. Similarly, central administration of drugs that inhibit the synthesis of eicosanoids, hydrocortisone, diclofenac and paracetamol, also attenuated the pro-inflammatory effect of
bradykinin. The findings indicate that the inflammation-promoting effect of centrally administered bradykinin involves the central prostaglandin and cholinergic neurotransmitter systems.

L11 ANSWER 17 OF 39 MEDLINE
AN 88274770 MEDLINE
DN 88274770
TI Natriuretic and vasodilating activities of intrarenally **administered** atriopeptin II, substance P and **bradykinin** in the dog.
AU DeFelice A F; Brousseau A
CS Sterling-Winthrop Research Institute, Department of Pharmacology, Rensselaer, New York..
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1988 Jul) 246 (1) 183-8.
Journal code: JP3. ISSN: 0022-3565.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198810
AB The mechanism of the diuretic effect of atrial natriuretic factor is unclear. In this study, we compared the renal vasodilating and diuretic effects of renal arterial infusions of rat atriopeptin II in anesthetized dogs to see if natriuresis and increases in total renal blood flow were associated. The vasodilators substance P and bradykinin also were tested. Volume (V), Na+ and K+ concentration and Na+ and K+ content (UNaV; UkV) of urine from the infused and contralateral kidneys (IK; CK) were measured as well as mean total renal blood flow (RBF) of the IK. Atriopeptin II (30-1000 ng/kg/min) slightly promoted RBF by up to 20%, but raised V, UNaV and UkV by a maximum of 79, 190 and 100%, respectively. Substance P (0.01-30 ng/kg/min) raised RBF of IK by a maximum of 59%, reduced mean blood pressure by 26% and had a biphasic effect on IK excretion: V, UNaV and UkV were increased maximally by 105, 154 and 42% at 1.0 ng/kg/min, whereas progressively less diuresis, natriuresis and kaliuresis occurred at higher (hypotensive) doses. CK excretion was unchanged. Bradykinin (1-100 ng/kg/min) raised RBF, V, UNaV, and UkV of IKs by a mean maximum of 97, 70, 201 and 47%, respectively, with no changes in mean blood pressure or CK excretion. The natriuretic and hyperemic effects of nonhypotensive doses of each peptide were significantly correlated. However, atriopeptin II uniquely promoted Na+ excretion, but not RBF at the lowest dose tested, and, after 10 min washout of the 1000-ng/kg/min dose, and did not appreciably promote RBF after 10 min of infusion. It also caused CK diuresis.(ABSTRACT TRUNCATED AT 250 WORDS)

L11 ANSWER 18 OF 39 MEDLINE
AN 88199221 MEDLINE
DN 88199221
TI Hyperthermic effect of centrally **administered bradykinin** in the rat: role of prostaglandins and serotonin.
AU Rao P J; Bhattacharya S K
CS Department of Pharmacology, Banaras Hindu University, Varanasi, India..
SO INTERNATIONAL JOURNAL OF HYPERTHERMIA, (1988 Mar-Apr) 4 (2) 183-9.
Journal code: IJY. ISSN: 0265-6736.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198808
AB Intracerebroventricularly administered bradykinin (2.5, 5 and 10 micrograms/rat) produced a dose-related increase in the rectal temperature of adult Wistar strain albino rats. The bradykinin-induced hyperthermia was significantly attenuated following pretreatment of the animals with pharmacological agents which selectively reduce rat brain serotonin or prostaglandin (PG) activity. These findings, and those of earlier reports emanating from this laboratory which indicate that centrally administered bradykinin augments rat brain serotonin and PGE2 activity, suggest the involvement of PGs and serotonin in the hyperthermic action of bradykinin in this species.

L11 ANSWER 19 OF 39 MEDLINE
AN 88031464 MEDLINE
DN 88031464
TI Antinociceptive effect of intracerebroventricularly **administered bradykinin** in rat: role of putative neurotransmitters.

AU Rao P J; Bhattacharya S K
SO INDIAN JOURNAL OF [redacted]PERIMENTAL BIOLOGY, (1987 May) [redacted] (5) 315-8.
Journal code: GIZ. ISSN: 0019-5189.
CY India
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 198802

L11 ANSWER 20 OF 39 MEDLINE
AN 87093460 MEDLINE
DN 87093460
TI Effects of intracerebroventricular **administration** of **bradykinin** on rat brain serotonin and prostaglandins.
AU Bhattacharya S K; Rao P J; Brumleve S J; Parmar S S
SO RESEARCH COMMUNICATIONS IN CHEMICAL PATHOLOGY AND PHARMACOLOGY, (1986 Dec)
54 (3) 355-66.
Journal code: R62. ISSN: 0034-5164.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198704
AB Intracerebroventricular (ICV) administration of bradykinin (5, 10 and 20 micrograms) produced a dose-related increase in the concentration of serotonin in rat brain. The maximum increase was observed after 15 min of bradykinin administration. Thereafter, the augmented levels of serotonin declined and tended to come to normal value after 60 min. Bradykinin (20 micrograms) significantly increased the concentrations of serotonin specifically in cortex, hypothalamus, midbrain and pons-medulla but not in
cerebellum and spinal cord. The time course of increase and subsequent decline of regional concentrations of serotonin in brain were similar to that noted with bradykinin-induced changes in serotonin levels in whole brain. Bradykinin (5, 10 and 20 mg, ICV) increased the concentration of prostaglandin E2 (PGE2) but not of PGF2 alpha of rat brain. The time course of bradykinin-induced changes in PGE2 concentrations were similar to the effects of bradykinin on the levels of serotonin in rat brain. The inhibitors of PG synthesis, hydrocortisone, diclofenac and paracetamol, antagonized the bradykinin-induced increase of serotonin in rat brain. These results have provided support for the contention that PGs may presumably mediate some of the central actions of bradykinin and that bradykinin-induced augmentation of central serotonergic activity could possibly account for PGE2-induced modulation of rat brain serotonin.

L11 ANSWER 21 OF 39 MEDLINE
AN 83079679 MEDLINE
DN 83079679
TI Effects of cardiac **administration** of **bradykinin** on thoracic spinal neurons in the cat.
AU Weber R N; Blair R W; Foreman R D
NC HL-22732 (NHLBI)
HL07430 (NHLBI)
HL-00557 (NHLBI)
SO EXPERIMENTAL NEUROLOGY, (1982 Dec) 78 (3) 703-15.
Journal code: EQF. ISSN: 0014-4886.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198304

L11 ANSWER 22 OF 39 MEDLINE
AN 82001526 MEDLINE
DN 82001526

TI Thermoregulatory effects of centrally **administered** bombesin, **bradykinin**, and methionine-enkephalin.
AU Francesconi R; Mager M
SO BRAIN RESEARCH BULLETIN, (1981 Jul) 7 (1) 63-8.
Journal code: B5M. ISSN: 0361-9230.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198201
AB Bombesin (BO, 100 ng), bradykinin (BR, 10 microgram), or methionine-enkephalin (EN, 10 microgram) was administered intracerebroventricularly to adult male rats at an environmental temperature of 4 degrees C, 22 degrees C, or 35 degrees C, and rectal (Tre) and tail-skin (Tsk) temperatures were monitored for 5 hours. At 4 degrees C and 22 degrees C BO-treated animals developed acute hypothermia (max delta Tre=-3.25 degrees C and -2.71 degrees C, respectively) which persisted for 2 hours (p less than 0.05). At 22 degrees C and at 300 min post-injection, BO-treated animals became significantly (p less than 0.05) hyperthermic (deltaTre = +1.28 degrees C) when compared to controls. While BR had no effects at 22 degrees C, en-injected rats demonstrated significant (p less than 0.05) hyperthermia from 180 min through 300 min (delta Tre=+1.40 degrees C). At 22 degrees C both BO and, surprisingly, EN increased Tsk (e.g. delta Tsk =+ 3.49 degrees C and + 2.01 degrees C at 60 min). At 35 degrees C EN elicited hyperthermia which was significantly (p less than 0.05) increased from time 0 at all sampling time (mean delta Tre =+ 1.85 degrees C) and from control levels at 300 min (delta Tre =+1.07 degrees C, p less than 0.05). BO again caused a significant (p less than 0.05, BO vs control, 30 min) decrement (delta Tre =-1.22 degrees C) followed by increments (p less than 0.05) from 12-0-300 min. We conclude that the hypothermic effect of BO is dependent upon environmental temperature, partially caused by vasodilation, and possible biphasic in nature; EN treatment generally elicits hyperthermia under these conditions while BR produced no effects on thermoregulation.

L11 ANSWER 23 OF 39 MEDLINE
AN 81193899 MEDLINE
DN 81193899
TI Effects of endogenous peptides **administered** intracerebroventricularly on acetic acid-induced writhing syndrome in mice. I. Neurotensin, **bradykinin**, somatostatin and methionine-enkephalin.
AU Kudo T; Oheda N; Kotani Y; Inoki R
SO OSAKA DAIGAKU SHIGAKU ZASSHI. JOURNAL OF THE OSAKA UNIVERSITY DENTAL SOCIETY, (1980 Dec) 25 (2) 264-72.
Journal code: JJ2.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
FS Dental Journals; Dental
EM 198109

L11 ANSWER 24 OF 39 MEDLINE
AN 81065053 MEDLINE
DN 81065053
TI Effects of intracoronary **administration** of **bradykinin** on the impulse activity of afferent sympathetic unmyelinated fibers with left ventricular endings in the cat.
AU Lombardi F; Della Bella P; Casati R; Malliani A

SO CIRCULATION RESEARCH, (1981 Jan) 48 (1) 69-75.
Journal code: DAJ[redacted]SSN: 0009-7330.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198104
AB In anesthetized and artificially ventilated cats, we recorded the impulse activity of 23 afferent sympathetic unmyelinated fibers with left ventricular endings, dissected from the left sympathetic rami T3 and T4. All fibers displayed a spontaneous discharge at a rate of 0.79 +/- 0.2 (mean +/- SE) impulses/sec. During constriction of the thoracic aorta, the discharge increased to 1.92 +/- 0.2 impulses/sec. During myocardial ischemia, produced by interruption of left main coronary artery perfusion, supplied through an extracorporeal pump, the impulse activity increased to 1.73 +/- 0.3 impulses/sec. The mean latency for this excitation was 16.5 +/- 1.5 sec. The intracoronary administration of bradykinin (5 and 10 ng/kg) elicited a marked increase in impulse activity that, following 5 ng/kg, reached 2.06 +/- 0.2 impulses/sec, after a latency of 18 +/- 2 sec and in absence of significant hemodynamic changes. Myocardial ischemia and bradykinin never revealed the existence of silent afferent fibers included in the split nerve strand. The results obtained with this experimental model indicate that the ventricular endings of these afferent sympathetic unmyelinated fibers act as "polymodal" receptors. We hypothesize that the peripheral mechanism for cardiac nociception involves intensive excitation of fibers discharging spontaneously and not recruitment of silent fibers which are purely nociceptive in function.

L11 ANSWER 25 OF 39 MEDLINE
AN 74169504 MEDLINE
DN 74169504
TI Effects of intravenous **administration** of slow-reacting substance of anaphylaxis, histamine, **bradykinin**, and prostaglandin F2alpha on pulmonary mechanics in the guinea pig.
AU Drazen J M; Austen K F
SO JOURNAL OF CLINICAL INVESTIGATION, (1974 Jun) 53 (6) 1679-85.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 197409

L11 ANSWER 26 OF 39 MEDLINE
AN 74010702 MEDLINE
DN 74010702
TI Mechanism of edema formation in canine forelimbs by locally **administered bradykinin**.
AU Kline R L; Scott J B; Haddy F J; Grega G J
SO AMERICAN JOURNAL OF PHYSIOLOGY, (1973 Nov) 225 (5) 1051-6.
Journal code: 3U8. ISSN: 0002-9513.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197401

L11 ANSWER 27 OF 39 MEDLINE
AN 73049423 MEDLINE

DN 73049423
TI [Augmentation of t[redacted]tonus of the muscles of the ne[redacted] during **administration** of **bradykinin** into the subarachnoid spaces in rats].
Augmentation du tonus des muscles de la nuque lors de l'introduction de la
bradykinine dans les espaces sous-arachnoidiens du rat.
AU Damas J
SO ELECTROMYOGRAPHY AND CLINICAL NEUROPHYSIOLOGY, (1972 Jul-Sep) 12 (3) 267-72.
Journal code: EEN. ISSN: 0301-150X.
CY Belgium
DT Journal; Article; (JOURNAL ARTICLE)
LA French
EM 197303

L11 ANSWER 28 OF 39 MEDLINE
AN 72188037 MEDLINE
DN 72188037
TI [The influence of intraventricularly **administered** angiotensin II, **bradykinin** and eledoisin on arterial blood pressure, respiration and electrocardiogram].
Der Einfluss von intraventrikular verabreichten Angiotensin II, **Bradykinin** und Eledoisin auf den arteriellen Blutdruck, die Atmung und das Elektrokardiogramm.
AU Cuparencu B; Ticsa I; Safta L; Csutak V; Mocan R
SO ACTA BIOLOGICA ET MEDICA GERMANICA, (1971) 27 (2) 435-41.
Journal code: 0E6.
CY GERMANY, EAST: German Democratic Republic
DT Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals
EM 197209

L11 ANSWER 29 OF 39 MEDLINE
AN 72180575 MEDLINE
DN 72180575
TI Selective inhibition by mepacrine of the release of "rabbit aorta contracting substance" evoked by the **administration** of **bradykinin**.
AU Vargaftig B B; Hai N D
SO JOURNAL OF PHARMACY AND PHARMACOLOGY, (1972 Feb) 24 (2) 159-61.
Journal code: JNR. ISSN: 0022-3573.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197209

L11 ANSWER 30 OF 39 MEDLINE
AN 72178689 MEDLINE
DN 72178689
TI [Research on neuro-humoral regulation of the circulation. (Study of changes induced in arterial pressure and heart activity by **administration** of **bradykinin** in circulatory areas of the femoral and carotid arteries)].
Ricerche sulla regolazione neuro-umorale della circolazione. Studio delle modificazioni indotte sulla pressione arteriosa e sull'attivit`a cardiaca dall'introduzione di bradichinina nei distretti circolatori femorale e carotideo.
AU Tallarida G; Baldoni F; Semprini A; Bossi G
SO MINERVA CARDIOANGIOLOGICA, (1972 May) 20 (5) 272-81.
Journal code: N2M. ISSN: 0026-4725.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)

LA Italian
EM 197209

L11 ANSWER 31 OF 39 MEDLINE
AN 71150369 MEDLINE
DN 71150369
TI Enzymology of the refractory media of the eye. X. Effects of topically **administered bradykinin**, amine releasers, and pargyline on aqueous humor dynamics.
AU Zeller E A; Shoch D; Czerner T B; Hsu M Y; Knepper P A
SO INVESTIGATIVE OPHTHALMOLOGY, (1971 Apr) 10 (4) 274-81.
Journal code: GWH. ISSN: 0020-9988.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197107

L11 ANSWER 32 OF 39 MEDLINE
AN 71136661 MEDLINE
DN 71136661
TI The effects of the intraventricular **administration** of angiotensin II, **bradykinin** and eledoisin on the arterial blood pressure, respiratory movements and electrocardiogram.
AU Cuparencu B; Ticsa I; Safta L; Csutak V; Mocan R
SO REVUE ROUMAINE DE PHYSIOLOGIE, (1969) 6 (3) 213-20.
Journal code: T3K. ISSN: 0035-399X.
CY Romania
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197106

L11 ANSWER 33 OF 39 MEDLINE
AN 71075067 MEDLINE
DN 71075067
TI Effect of local intraarterial **administration** of **bradykinin** and hydergine in obstructive arterial disease.
AU Erikson U
SO ACTA RADIOLOGICA: DIAGNOSIS, (1970 Nov) 10 (6) 449-57.
Journal code: 1XX. ISSN: 0567-8056.
CY Sweden
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197104

L11 ANSWER 34 OF 39 MEDLINE
AN 71016655 MEDLINE
DN 71016655
TI [Behavior of vascular resistance of the hind leg of the rabbit after **administration** into the femoral artery of microdoses of **bradykinin**. Study of the dose-effect relationship].
Comportamento delle resistenze vascolari nell'arto posteriore del coniglio
dopo somministrazione in arteria femorale di microdosi di bradichinina. Studio del rapporto dose-effetto.
AU Cassone R; Tallarida G; Lucisano V; Semprini A; Condorelli M
SO BOLLETTINO - SOCIETA ITALIANA BIOLOGIA SPERIMENTALE, (1969 Nov 30) 45 (22)
1395-9.
Journal code: ALS. ISSN: 0037-8771.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA Italian

FS Priority Journals
EM 197101

L11 ANSWER 35 OF 39 MEDLINE
AN 69155862 MEDLINE
DN 69155862
TI Vocalization response of puppies to intra-arterial **administration** of **bradykinin** and other algesic agents, and mode of actions of blocking agents.
AU Taira N; Nakayama K; Hashimoto K
SO TOHOKU JOURNAL OF EXPERIMENTAL MEDICINE, (1968 Dec) 96 (4) 365-77. Journal code: VTF. ISSN: 0040-8727.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 196907

L11 ANSWER 36 OF 39 MEDLINE
AN 67200863 MEDLINE
DN 67200863
TI Influence of intravascular and topically **administered** **bradykinin** on microcirculation of several tissues.
AU Hyman C; Paldino R L
SO BIBLIOTHECA ANATOMICA, (1967) 9 38-45. Journal code: 9RK. ISSN: 0067-7833.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 196711

L11 ANSWER 37 OF 39 MEDLINE
AN 65059142 MEDLINE
DN 65059142
TI [CLINICO-RADIOLOGIC CONSIDERATIONS ON THE EFFECTS OF **BRADYKININ** **ADMINISTERED** INTRAARTERIALLY].
CONSIDERAZIONI CLINICO-RADIOLOGICHE SUGLI EFFETTI DELLA BRADICHININA SOMMINISTRATA PER VIA ENDOARTERIOSA.
AU DEIDDA C; NUTI A; CORSI C; BRUNETTI S
SO RIVISTA CRITICA DI CLINICA MEDICA, (1964 JUN) 64 251-75. Journal code: TIP. ISSN: 0048-833X.
CY Italy
LA Italian
FS OLDMEDLINE
EM 196505

L11 ANSWER 38 OF 39 MEDLINE
AN 62180736 MEDLINE
DN 62180736
TI Plasmakinin levels in man after intravenous and intraarterial **administration** of synthetic and natural **bradykinin**.
AU SICUTERI F; PERITI P; ANSELMI B; FANCIULLACCI M
SO Boll Soc Ital Biol Sper, (1963 Mar 15) 39 314-8.
LA Italian
FS OLDMEDLINE
EM 196312

L11 ANSWER 39 OF 39 MEDLINE
AN 60127928 MEDLINE
DN 60127928
TI Changes of behavior after intracerebral **administration** of **bradykinin**.
AU CAPEK R
SO Cesk Fysiol, (1960 May) 9 283-4.

EM 199506

AB Angiotensin conve[redacted]ng enzyme inhibitors (ACEIs) a[redacted]a cornerstone of treatment of hypertension and heart failure yet the[redacted] mechanism of action is still debated. This study was designed to test whether the ACEI captopril increases skin microvascular blood flow by a bradykinin-dependent mechanism. Local changes in microvascular blood flow were measured in the skin of rabbits and of human volunteers using a laser Doppler flow probe. Captopril injected intradermally increased skin blood flow over the dose range of 10(-12)-10(-8) mol site in rabbits and humans. In both species the response was abolished by coinjecting either a **nitric oxide synthase** (**NOS**) inhibitor or a cyclooxygenase inhibitor. Intradermal bradykinin also increased rabbit skin microvascular blood flow; at 10(-11) mol site it increased mean +/- SE basal blood flow by 88 +/- 12%. The responses to bradykinin or captopril were abolished by coinjecting a bradykinin antagonist, a specific **bradykinin B2 receptor antagonist**, or inhibitors of **NOS** or cyclooxygenase. Injecting a specific angiotensin II receptor antagonist at a dose that antagonized the constrictor effects of exogenous angiotensin II did not cause a significant increase in rabbit skin blood flow. This suggests that endogenous angiotensin II does not influence microvascular blood flow in this model. The results indicate that captopril increases skin microvascular blood flow in rabbits and humans secondary to an increase in endogenous tissue bradykinin; this stimulates B2 receptors with subsequent release of prostaglandins and nitric oxide. ACEIs may increase microvascular perfusion by a bradykinin-dependent mechanism.

ANSWER 142 OF 243 MEDLINE

AN 96428957 MEDLINE

DN 96428957

TI Bradykinin and changes in microvascular permeability in the hamster cheek pouch: role of nitric oxide.

AU Feletou M; Bonnardel E; Canet E

CS Department de Pneumologie, Institut de Recherches Servier, Suresnes, France.

SO BRITISH JOURNAL OF PHARMACOLOGY, (1996 Jul) 118 (6) 1371-6.
Journal code: B00. ISSN: 0007-1188.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199704

EW 19970402

AB 1. The objective of this study in the hamster cheek pouch was to investigate the role of nitric oxide in bradykinin-induced microvascular leakage. The cheek pouch microcirculatory bed of the anaesthetized hamster was directly observed under microscope and vascular leakage was evidenced by dextranfluorescein isothiocyanate (FITC-dextran) extravasation. 2. Bradykinin superfusion (but not [des-Arg9]-bradykinin up to 3 x 10(-6) M) induced an increase in microvascular permeability (log EC50: -6.5 +/- 0.4) which was exclusively located on the post-capillary venule. Plasma extravasation was blocked by intravenous pretreatment with Hoe 140, a **bradykinin B2 receptor antagonist** (estimated log ID50: -9.5 +/- 0.2). 3. The effects of bradykinin (3 x 10(-7) M) superfusion were partially but significantly inhibited by indomethacin (10(-5) M, $P < 0.05$) and abolished by pretreatment with L-nitro-arginine (L-NOARG; 10(-5) M). 4. Acetylcholine (10(-6) M, which releases endothelial nitric oxide (NO), and sodium nitroprusside (10(-6) M, a nitrovasodilator) superfusion did not induce any changes in permeability, per se. Cromakalim (10(-5) M, a potassium channel opener) superfusion induced a moderate but significant plasma extravasation. 5. The effects of bradykinin, blocked by L-NOARG pretreatment, were restored by the co-perfusion of either sodium nitroprusside or cromakalim. Conversely vasoconstriction, produced by a stable analogue of thromboxane A2 (U46619, 3 x 10(-7) M), inhibited the increase in permeability produced by bradykinin. 6. The measurement of arteriolar diameter showed that bradykinin induced a vasodilatation which was blocked by L-NOARG. L-NOARG in itself was a powerful vasoconstrictor. Sodium nitroprusside and cromakalim, in the presence of L-NOARG, were able to restore the inhibited vasodilator response to bradykinin. 7. These results suggest: (1) bradykinin-induced microvascular leakage is mediated by bradykinin B2 receptor activation; (2) the increase in permeability is due to two different independent phenomena, i.e. post-capillary venular endothelial gap formation and arteriolar vasodilatation which increases the post-capillary venular transmural pressure: (3) NO is only involved in the arteriolar dilatation component of the bradykinin-induced increase in microvascular permeability.

L8 ANSWER 337 OF 417 MEDLINE
AN 75171890 MEDLINE
DN 75171890
TI Effect of intracerebroventricular bradykinin and related peptides on rabbit operant behavior.
AU Melo J C; Graeff F G
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1975 Apr) 193 (1) 1-10.
Journal code: JP3. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197510
AB The dose-effect relationships of intraventricularly injected bradykinin, Gly-Arg-Met-Lys-bradykinin (GAML-bradykinin), synthetic substance P and angiotensin II on lever-lifting behavior of rabbits in a variable-interval (VI) 72-second schedule of sweetened water presentation were determined. All peptides used caused dose-dependent decreases in overall rates of VI responding during the experimental session in the following order of potency: angiotensin II greater than bradykinin = substance P greater than GAML-bradykinin. The angiotensin II dose-effect curve was less steep than those of the other peptides. The administration of nearly equimolar doses of the bradykinin potentiating peptides, BPP5a and BPP9a, slightly decreased overall VI response rates and caused a 10- to 20-fold potentiation of the rate-decreasing effect of bradykinin on VI responding.
Both angiotensin II and bradykinin caused pauses in responding of dose-dependent duration at the beginning of the experimental session that were followed by normal VI responding. The effect of GAML-bradykinin on VI performance was similar to that of bradykinin and angiotensin II but had a delay of onset of 3 to 6 minutes. In contrast, substance P caused actual decreases in response output and pauses of variable duration interspersed between periods of regular VI responding. At the doses used, both bradykinin-potentiating peptides caused uniform decreases in VI responding throughout the experimental session. Gross behavioral changes caused by the peptides were also observed. After the intraventricular injection of bradykinin or GAML-bradykinin, rabbits showed decreased motility, ptosis, miosis and lowered ears; after angiotensin II, animals remained motionless but with wide open eyes, fully raised ears and no miosis. In turn, substance P caused restlessness and increased locomotion. These results together with reported evidence on other powerful central actions of bradykinin, angiotensin and substance P and on the existence of components of their releasing and destroying enzymatic systems in the brain suggest that linear peptides may play a role in the functioning of the central nervous system.

8 ANSWER 340 OF 417 MEDLINE
AN 75139690 MEDLINE
DN 75139690
TI The effects of trypsin digested globulin degradation products (TDPG) on the activity of central nervous system.
AU Wisniewski K; Tarasiewicz S; Mackowiak J; Buczko W; Moniuszko-Jakoniuk J
SO PHARMACOLOGY, (1974) 12 (6) 321-30.
Journal code: P43. ISSN: 0031-7012.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197508
AB Studies on trypsin-digested globulin degradation products given to rats intraperitoneally or intraventricularly, revealed psychodepressive effects on the central nervous system. Peptides with a molecular weight of approximately 1,3000 were the most active.

L8 ANSWER 341 OF 417 MEDLINE
AN 75135124 MEDLINE
DN 75135124
TI Central site of the hypertensive action of bradykinin.
AU Correa F M; Graeff F G
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1975 Mar) 192 (3) 670-6.
Journal code: JP3. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197508
AB The intraventricular injection of 1 mug of bradykinin (BK) in rats anesthetized with urethane (1.5 g/kg i.p.) caused an increase in mean arterial blood pressure with little or no change in pulse pressure or heart rate. A similar hypertensive response followed the local administration of 0.5 mug of BK at the pars ventralis of the lateral septal area, whereas local application at other subcortical regions, known to be involved in cardiovascular regulation, caused no effect. Injections of 0.5 or 1 mug of synthetic substance P or 1 mug of 9-desarginine-bradykinin at the pars ventralis of the lateral septal area caused no change in blood pressure. In addition, bilateral electrolytical lesions placed in the lateral septal area either markedly reduced or completely blocked the pressor response to intraventricular BK. These results suggest that the pars ventralis of the lateral septal area is involved in the pressor action of BK in the central nervous system. They also indicate that this brain region responds fairly specifically to BK and that local vascular changes are unlikely to be involved in the mediation of the central action of BK.

L1 ANSWER 18 OF 18 REGISTRY COPYRIGHT 2000 ACS
RN 2149-70-4 REGISTRY
CN L-Ornithine, N5-[imino(nitroamino)methyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ornithine, N5-(nitroamidino)-, L- (8CI)
OTHER NAMES:
CN (+)-NG-Nitroarginine
CN **.omega.-Nitro-L-arginine**
CN .omega.-Nitroarginine
CN L-Arginine, .omega.-nitro-
CN L-Arginine, NG-nitro-
CN L-NG-Nitroarginine
CN **N.omega.-Nitro-L-arginine**
CN **N.omega.-Nitro-L-arginine**
CN **NG-Nitro-L-arginine**
CN NG-Nitroarginine
CN **Nitro-L-arginine**
CN Nitroarginine
CN NOLA
FS STEREOSEARCH
DR 13855-78-2, 126265-23-4, 38733-00-5
MF C6 H13 N5 O4
CI COM
LC STN Files: AGRICOLA, AIDSLINE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.

L8 ANSWER 10 OF 40 CA COPYRIGHT 2001 ACS
AN 120:125955 CA
TI EDRF-like actions of homoarginine oligopeptide
AU Gu, MingDi; Peng, ShiQi; Jiang, XiuRong; Guo, XueQing; Cai, MengShen; Zhang, Li; Dong, ShuYun; Zhang, LianYuan; Tang, ChaoShu
CS Nat. Lab. Nat. Bionimetic Drugs, Beijing Med. Univ., Beijing, 100083, Peop. Rep. China
SO Prog. Nat. Sci. (1993), 3(2), 155-9
CODEN: PNASEA
DT Journal
LA English
AB Based on the advances in research on endothelium derived relaxing factor (EDRF), a homoarginine oligopeptide was designed and synthesized. Its vasodilation and depressor actions on Wistar rats were obsd., and the effects have been found to be independent of the vascular endothelium. The strong EDRF-like action of the oligopeptide provides an excellent lead compd. for structure-activity relationship (SAR) studies of homoarginine and derivs.
CC 2-10 (Mammalian Hormones)
ST EDRF **arginine dipeptide**; endothelium derived relaxing factor homoarginine dipeptide
IT Blood pressure
(arginine and arginylarginine effect on, EDRF-like activity in relation to)
IT Heart
(rate of, arginine and arginylarginine effect on, EDRF-like activity in relation to)
IT Artery
(aorta, endothelium, vasoconstriction by arginine and arginylarginine independent from)
IT 74-79-3, L-Arg, biological studies
RL: BIOL (Biological study)
(blood pressure and heart rate response to, EDRF-like actions of arginylarginine in relation to)
IT 90880-94-7, EDRF
RL: BIOL (Biological study)
(homoarginine oligopeptide biol. activity in comparison with)
IT 15483-27-9P, Arg-Arg
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and EDRF-like activity of)
IT 79141-07-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deprotection of)
IT 153088-42-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction with protected arginine)

0 ANSWER 7 OF 7 CA COPYRIGHT 2001 ACS
AN 115:252941 CA
TI Inhibition of the release of endothelium-derived relaxing factor in vitro and in vivo by dipeptides containing NG-nitro-L-arginine
AU Thiemermann, Christoph; Mustafa, Marina; Mester, P. Achim; Mitchell, Jane A.; Hecker, Markus; Vane, John R.
CS Med. Coll., St. Bartholomew's Hosp., London, EC1M 6BQ, UK
SO Br. J. Pharmacol. (1991), 104(1), 31-8
CODEN: BJPCBM; ISSN: 0007-1188
DT Journal
LA English
AB It was shown that dipeptides contg. NG-nitro-L-arginine (NO2Arg) inhibit the biosynthesis of endothelium-derived relaxing factor (EDRF) in vitro and in vivo. In anesthetized rats, i.v. administration at 1-30 mg kg-1 of the Me ester of NO2Arg, NO2-Arg-L-phenylalanine (NO2Arg-Phe), L-alanyl-NO2Arg (Ala-NO2Arg), or NO2Arg-L-arginine (NO2Arg-Arg) produced dose-related increases in mean arterial blood pressure (MABP) which were unaffected by D-arginine (D-Arg; 20 mg kg-1 min-1 for 15 min), but prevented by co-infusions of L-arginine (L-Arg; 20 mg kg-1 min-1 for 15 min) or by their parent dipeptides. NO2Arg Me ester, NO2Arg-Phe Me ester, or Ala-NO2Arg Me ester (10 mg kg-1, i.v.) also inhibited the redn. in MABP caused by the endothelium-dependent vasodilator, acetylcholine (30 .mu.g kg-1 min-1 for 3 min), but not those inhibited by glyceryl trinitrate (20 .mu.g kg-1) min-1 for 3 min) or iloprost (6 .mu.g kg-1 min-1 for 3 min) which act directly on the vascular smooth muscle. Moreover, NO2Arg Me ester, NO2Arg-Phe Me ester, or NO2Arg-Arg Me ester (100 .mu.M) inhibited the acetylcholine-induced relaxation of rabbit aortic strips, and NO2Arg-Phe Me ester (30 .mu.M) blocked the stimulated (bradykinin, 30 pmol) release of EDRF from bovine aortic endothelial cells grown on microcarrier beads. In endothelial cells grown in L-Arg-deficient medium, L-Arg-contg. dipeptides such as L-Arg-L-Phe, L-Ala-L-Arg, or L-Arg-L-Arg increased both the basal and simulated release of EDRF. Moreover, the L-Arg contg. dipeptides, but not their NO2Arg analogs, were rapidly cleaved by these cells. Thus, dipeptides contg. NO2Arg can directly interfere with the biosynthesis of EDRF in vitro and in vivo. Moreover, the potentiation of EDRF release from endothelial cells deprived of L-Arg by dipeptides contg. L-Arg suggests that such peptides may serve as an addnl. or alternative substrate for the biosynthesis of EDRF.
CC 13-7 (Mammalian Biochemistry)
ST nitroarginine peptide endothelium derived relaxing factor
IT Artery, metabolism
(aorta, endothelium, arginine and nitroarginine peptides metab. by)
IT Peptides, biological studies
RL: BIOL (Biological study)
(di-, nitroarginine-contg., EDRF release by aorta endothelium inhibition by)
IT 75691-50-8 137461-06-4 137461-07-5
RL: BIOL (Biological study)
(endothelium-derived relaxing factor release inhibition by, hemodynamics in rat in relation to)
IT 2047-13-4 15483-27-9, Arginyl-arginine 16709-12-9 104104-47-4 **137461-08-6** 137461-09-7
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metab. of, by vascular endothelium)
IT 90880-94-7, Endothelium-derived relaxing factor

RL: BIOL (Biological study)
(release of, ni[redacted]arginine-contg. peptides inhib[redacted]ion of)

L10 ANSWER 3 OF 7 CA COPYRIGHT 2001 ACS
AN 129:339884 CA
TI Inhibition of nitric oxide synthase isoforms by amino acids and dipeptides
IN Silverman, Richard B.; Huang, Hui; Zhang, Henry Q.
PA Northwestern University, USA
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9848826	A1	19981105	WO 1998-US7037	19980408
	W: AU, CA, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9872463	A1	19981124	AU 1998-72463	19980408

PRAI US 1997-45192 19970430
US 1997-62668 19971008
WO 1998-US7037 19980408
OS MARPAT 129:339884
AB Methods and compns. for inhibiting at least one isoform of nitric oxide synthase are provided. Pharmaceutical compns. include derivs. of arginine as well as dipeptides and dipeptide analogs that contain nitroarginine or another unnatural amino acid. Compns. can be used to selectively inhibit particular isoforms of nitric oxide synthase. N.omega.-propyl-L-arginine was a potent and selective competitive inhibitor of neuronal nitric oxide synthase (nNOS) from bovine brain. Its Ki for inhibition of nNOS is 3158 times lower than that for inhibition of recombinant murine macrophage NOS (iNOS) and 149 times lower than that for inhibition of recombinant bovine endothelial NOS (eNOS).
IC ICM A61K038-05
CC 1-12 (Pharmacology)
Section cross-reference(s): 7, 34, 63
ST nitric oxide synthase inhibitor dipeptide; amino acid inhibitor nitric oxide synthase
IT Peptides, biological studies
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amides, dipeptides; inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)
IT Peptidomimetics
(dipeptides; inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)
IT Peptides, biological studies
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(esters, dipeptides; inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)
IT Structure-activity relationship
(inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)
IT Neurons
Vascular endothelium
(nitric oxide synthase isoform of; inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)
IT Dipeptides

RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(unnatural amino acid-contg.; inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)

IT Amino acids, biological studies
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(unnatural; inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)

IT 63-91-2, Phenylalanine, biological studies 70-26-8, Ornithine 305-62-4, 2,4-Diaminobutanoic acid 515-94-6, 2,3-Diaminopropanoic acid 2149-70-4 66036-77-9 137433-32-0
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(in dipeptide; inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)

IT 125978-95-2, Nitric oxide synthase
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)

IT 2418-78-2P 2418-79-3P 2418-80-6P 2418-81-7P 2418-85-1P 47556-24-1P 50573-05-2P 55909-20-1P 57704-72-0P 63452-77-7P 70671-38-4P 104104-47-4P 137461-06-4P **137461-08-6P** 194083-57-3P 194083-58-4P 194083-59-5P 194083-60-8P 194083-61-9P 194083-62-0P 194083-63-1P 215605-47-3P 215605-58-6P 215605-61-1P 215605-63-3P 215605-65-5P 215605-67-7P 215605-68-8P 215605-70-2P 215605-82-6P 215605-85-9P 215605-90-6P 215605-97-3P 215606-02-3P 215606-07-8P 215606-11-4P 215606-14-7P 215606-17-0P 215606-20-5P 215606-23-8P 215606-25-0P 215606-28-3P 215606-31-8P 215606-34-1P 215606-37-4P 215606-39-6P 215606-43-2P 215606-48-7P 215606-51-2P 215606-53-4P 215606-55-6P 215606-57-8P 215606-59-0P 215606-61-4P 215606-65-8P 215606-67-0P 215606-69-2P 215606-72-7P 215606-75-0P 215606-78-3P 215606-80-7P 215606-83-0P 215606-86-3P 215606-89-6P 215606-94-3P 215606-96-5P 215607-00-4P 215607-01-5P 215607-04-8P 215607-06-0P 215607-09-3P 215607-11-7P 215607-13-9P 215607-15-1P 215607-16-2P 215607-17-3P 215607-19-5P 215607-21-9P 215607-23-1P 215607-25-3P 215607-27-5P 215607-29-7P 215607-31-1P 215607-32-2P 215607-34-4P 215607-35-5P 215607-36-6P 215607-37-7P 215607-40-2P 215607-43-5P 215607-46-8P 215607-49-1P 215607-50-4P 215607-51-5P 215607-52-6P 215607-53-7P 215607-54-8P 215607-55-9P 215607-56-0P 215607-57-1P 215607-58-2P 215607-59-3P 215607-60-6P 215607-61-7P 215607-62-8P 215607-63-9P 215607-64-0P 215607-65-1P 215607-66-2P 215607-67-3P 215607-68-4P 215607-69-5P 215607-70-8P 215607-71-9P 215607-72-0P 215607-73-1P 215607-74-2P 215607-75-3P 215607-76-4P 215607-77-5P 215607-78-6P 215607-79-7P 215607-80-0P 215607-81-1P 215607-82-2P 215607-83-3P 215607-84-4P 215607-85-5P 215607-86-6P 215607-87-7P 215607-88-8P 215607-89-9P 215607-90-2P 215607-91-3P 215607-92-4P 215607-93-5P 215607-94-6P 215607-95-7P 215607-96-8P 215607-97-9P 215607-98-0P 215607-99-1P 215608-00-7P 215608-01-8P 215608-02-9P 215608-03-0P 215608-04-1P 215608-05-2P 215608-06-3P 215608-07-4P 215608-08-5P 215608-09-6P 215608-10-9P 215608-12-1P 215608-14-3P 215608-15-4P 215608-16-5P 215608-17-6P 215608-18-7P 215608-98-3P 215608-99-4P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)

IT 2577-94-8, Methyl-L-arginine 88855-11-2 215605-72-4 215605-74-6 215605-75-7
RL: BAC (Biological activity or effector, except adverse); BPR (Biological

process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)

IT 215605-54-2
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)

IT 74-79-3D, L-Arginine, derivs.
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(inhibition of nitric oxide synthase isoforms by amino acids and dipeptides)